TO STUDY THE SPECTRUM OF RENAL DYSFUNCTION IN ADMITTED PATIENTS WITH LIVER CIRRHOSIS

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ABSTRACT

Introduction: Renal dysfunction is a common complication in patients of liver cirrhosis and of utmost clinical and prognostic relevance. Chances of development of acute kidney injury (AKI) are more in patients with cirrhosis than the non-cirrhotic population. Most common causes of AKI in cirrhosis include pre-renal AKI, the hepatorenal syndrome type of AKI, intrinsic and post renal type of AKI. Differentiation is important as treatment and prognosis differs for each type of AKI.

Materials & methods: This study was an observational study which included 100 consecutive patients of age $\geq$ 18 years admitted in Dayanand Medical College and Hospital, Ludhiana with liver cirrhosis & were found to have renal dysfunction on admission. Aim was to study the clinical profile of renal dysfunction in admitted patients with liver cirrhosis. Baseline clinical, laboratory and radiological data were recorded to infer the type of AKI and outcome at the end of hospital stay was recorded in terms of recovery of AKI and mortality outcome.

Results: The most common type of acute renal dysfunction observed was Pre- renal (56%), followed by Intrinsic (26%), HRS (16%), post renal (2%). At the end of hospital stay, renal functions recovered completely in majority of patients (64%), recovered partially in 12 % of the patients, and did not recover in 24% of the patients. In terms of mortality outcome at the end of hospital stay, 73% patients survived and were discharged whereas 27 % of the patients of liver cirrhosis admitted with acute renal dysfunction expired. Maximum mortality was seen with intrinsic type of AKI (53.8%), followed by post renal AKI (50%) and HRS (37.5%). Minimum mortality was seen with pre-renal AKI (10.7%).

Conclusion: The etiology of renal diseases in the cirrhotic patients is varied. This study analysed data of the complete spectrum of renal disorders among hospitalized patients with cirrhosis which helps in early recognition of the type of acute kidney injury so that timely healthcare interventions can be done to prevent mortality and morbidity.

Keywords: liver cirrhosis, acute kidney injury, pre renal acute kidney injury, hepatorenal syndrome, intrinsic acute kidney injury, post renal acute kidney injury.

ABBREVIATION

ADQI	Acute Dialysis Quality Initiative
AKIN	Acute Kidney Injury Network
ATN	Acute tubular necrosis
AVP	Arginine vasopressin
ACLF	Acute-on-chronic liver failure
ABG	Arterial Blood Gas analysis
CLD	Chronic liver disease
CBC	Complete Blood Count
CXR	Chest X Ray
C/S	Culture/Sensitivity
CR	Completely Recovered
CTP	Child Turcotte Pugh
ECG	Electrocardiography
ESR	Erythrocyte Sedimentation Rate
F	Female
FENa	Fractional excretion of urinary sodium
GFR	Glomerular filtration rate
GI	Gastrointestinal
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HPF	High power field
HRS	Hepatorenal syndrome
ICA	International Club of Ascites
IgA	Immunoglobulin A
KDIGO	Kidney Disease Improving Global Outcome
LFT	Liver Function Tests
LPS	Lipopolysaccharides
M	Male
MELD	Model for End Stage Liver Disease
NASH	Non Alcoholic Steatohepatitis
NR	Not Recovered

PR	Partially Recovered
PTI/INR	Prothrombin Time/ International Normalised Ratio
RAAS	Renin-angiotensin-aldosterone system
RBC	Red Blood Cells
RBS	Random Blood Sugar
RFT	Renal Function Tests
SBP	Spontaneous bacterial peritonitis
S. Cr.	Serum Creatinine
SD	Standard deviation
SIRS	Systemic inflammatory response syndrome
Std.	Standard
TLR4	Toll-like receptor 4
TNF-a	Tumor Necrosis Factor – Alpha
UPCR	Spot Urine Protein Creatinine Ratio
USG	Ultrasound

KEY TO MASTER CHART

ABH	Altered Bowel Habits
AD	Abdominal Distension
AKI	Acute Kidney Injury
Alb	Albumin
ALD	Alcohol Related Disease
ALP	Alkaline Phosphatase
AS	Altered Sensorium
B	Bilirubin
CAD	Coronary Artery Disease
C. diff	Clostridium difficile
CKD	Chronic Kidney Disease
Comp & Alt Med	Complementary and Alternative Medications
CR	Completely Recovered
Cr. Cl.	Creatinine Clearance
C/S	Culture/ Sensitivity
CTP	Child Turcotte Pugh Score
DM II	Diabetes Mellitus Type II
DUO	Decreased Urine Output
ET Secr	Endotracheal Secretions
FENa	Fractional Excretion of Sodium
GPE	General Physical Examination
Hb	Haemoglobin
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
H/M	Haemetemesis/ Malaena
HPF	High power field
HRS	Hepato Renal Syndrome
HTN	Hypertension
Int	Intrinsic type of AKI
K	Serum Potassium

MELD	Model for End stage Liver Disease
N	No
Na	Serum Sodium
NASH	Non Alcoholic Steato Hepatitis
N.D	Not Done
NR	Non Reactive/ Not Recovered
NSAIDs	Non Steroidal Anti Inflammatory Drugs
OHA	Oral Hypoglycemic Agents
PA	Pain Abdomen
P/A (FF)	Per Abdomen (Free Fluid)
PCT	Procalcitonin
Plt	Platelet count
Post	Post Renal type of AKI
PR	Partially Recovered
Pre	Pre Renal type of AKI
PTI/INR	Prothrombin Time/ International Normalised Ratio
RD	Recently Detected
SAAG	Serum Ascitic Albumin Gradient
SAH	Subarachnoid Haemorrhage
SBP	Spontaneous Bacterial Peritonitis
SGOT	Serum Glutamic Oxaloacetic Transaminase
SGPT	Serum Glutamic Pyruvic Transaminase
TLC	Total Leucocyte Count
UPCR	Spot Urine Protein Creatinine Ratio
U. Spot Na	Spot Urinary Sodium
VB	Variceal Bleed
VM	Viral Markers
Y	Yes

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INTRODUCTION

Cirrhosis is a global burden and is currently the 11th most common cause of death globally and is within the top 20 causes of disability-adjusted life years and years of life lost, accounting for 1.6% and 2.1% of the worldwide burden. [1]In 2017, cirrhosis caused more than 1·32 million deaths (440000 in females and 883000 in males) globally, compared with less than 899000 deaths in 1990. Deaths due to cirrhosis constituted 2·4% of total deaths globally in 2017 compared with 1·9% in 1990. [2]

Acute kidney injury (AKI) is a common event in the natural history of patients with cirrhosis, with an incidence rate varying from 14% to 50%.[3-5]

In patients with advanced cirrhosis and portal hypertension renal perfusion may be critically impaired as a consequence of systemic and splanchnic arterial vasodilatation and consecutive reduction in effective circulating blood volume [6]. As a result, patients with cirrhosis are prone to developing renal dysfunction.

Acute renal dysfunction is a common presentation and life threatening complication in patients with advanced cirrhosis hospitalized with acute decompensation, and is associated with increased morbidity and mortality. Acute renal failure in patients with cirrhosis is associated with an almost 8 fold increase risk of death.[7]

AKI has an estimated prevalence of approximately 20–50% among hospitalized patients with cirrhosis [8–11] and patients with cirrhosis are more likely to develop renal failure compared to individuals without liver disease [12].

A systemic review of studies which evaluated the predictors of survival in cirrhosis have reported that parameters of renal dysfunction (creatinine and blood urea nitrogen/azotemia) together with parameters of liver dysfunction (Child-Pugh score and its components) were important predictors of death in decompensated cirrhosis.[13]

The pivotal prognostic role of renal function in cirrhosis is reflected by the inclusion of serum creatinine (sCr) in the Model for End Stage Liver

Disease (MELD) Score, which is currently used for assessment of severity of liver disease and prioritization of patients with advanced liver disease for liver transplantation [14 -16].

Acute kidney injury (AKI), defined by a significant reduction in glomerular filtration rate (GFR) over a short time period, is a common and severe complication in patients with cirrhosis and is often triggered by a precipitating event (i.e. overdose of diuretics, large-volume paracentesis without albumin replacement, gastrointestinal bleeding, bacterial infections, etc.) [17]. AKI is associated with poor prognosis and represents an important predictor for short-term mortality in patients with cirrhosis [8,9,18-20] as the occurrence of AKI, irrespective of the underlying cause, is associated with reduced in-hospital, 3-mo and 1-year survival.[21]

Recent data has shown that much smaller increases (≥0.3 mg/dL) in creatinine, some of which occur below the 1.0 mg/Dl creatinine cut off for MELD point allocation, have significant prognostic implications.[22,23] The chance for recovery is partially related to the absolute change in creatinine, and unfortunately the risk for death does not completely abate even if patients experience resolution of their acute renal failure.[22]

AKI occurs in 11% of patients with upper gastrointestinal bleeding, in 34% of patients with spontaneous bacterial peritonitis (SBP), in 27% with bacterial infections other than SBP and in 40% to 49% of critically-ill patients with cirrhosis requiring intensive care support [12,18]. Furthermore, 24% of outpatients with cirrhosis develop some type of renal failure within one year of the first episode of ascites [19].

Within the spectrum of acute renal dysfunction in patients with cirrhosis, hepatorenal syndrome (HRS), which has been defined as a purely ‘‘functional” type of renal failure without significant changes in renal histology, carries the most ominous prognosis because it usually denotes a background of severe portal hypertension and circulatory dysfunction. The clinical characteristics of HRS are similar to prerenaluremia, but the condition does not respond to volume expansion. Prerenalazotemia has been documented as the underlying

factor of acute renal injury, which is reported to initiate HRS-type 1 and progress to acute tubular necrosis (according to the level of splanchnic vasodilation or renal hypoperfusion and the reduced cardiac output).[24,25] The standard of care clinical management for patients with HRS AKI is to exclude other etiologies of AKI, followed by volume expansion with human albumin solution and then the introduction of vasopressors. HRS-AKI is a diagnosis by exclusion and thus, often difficult to establish [26,27]. However, some 40% of patients treated for HRS AKI fail to respond.[28]

With a yearly incidence of 8–12%, HRS-AKI is quite common in decompensated cirrhosis with ascites [29–31]. A number of factors can precipitate HRS such as infections, alcoholic hepatitis, and bleeding. However, despite adequate treatment mortality is still about 60% and higher. [20,32,33]

In 2007, the International Club of Ascites (ICA) classified HRS into types 1and2 (HRS-1andHRS-2).[26] HRS-1 is characterised by a rapid deterioration of renal function that often occurs because of a precipitating event, while HRS-2 is a moderate and stable or slowly progressive renal dysfunction that often occurs without an obvious precipitant. Clinically, HRS-1 is characterised by acute renal failure while HRS-2 is mainly characterised by refractory ascites.

The early detection of the type of AKI and its treatment is life saving in most instances. There are very few studies documenting various renal disorders in patients with cirrhosis of liver. Majority of clinical studies focused their attention on HRS, which is mostly present in advanced stages of cirrhosis. However, other forms of renal disorders in cirrhotic patients have equal importance in view of their incidence and prognostic impact in such patients. Hence, the present study was carried out to analyze the profile of renal dysfunction in patients with cirrhosis.

This study will help us in documenting the common causes of renal involvement in liver cirrhosis and in planning further investigation and management of these patients.

AIMS AND OBJECTIVES OF THE STUDY

1. To study the clinical profile of renal dysfunction in admitted patients with liver cirrhosis.

REVIEW OF LITERATURE

The first reports of renal failure in the setting of cirrhosis of liver were from Europe and the United States in the late nineteenth century.[30]Hecker and Sherlock in 1956 gave the first detailed description of HRS. [34]Vesin[35] and Koppel et al.[36] later established the functional nature of this renal disease. Since then, the relationship between the liver and kidney functions has been an object of great research efforts.

EPIDEMIOLOGY

AKI occurs in 25% to 50% of cirrhotic patients admitted to the hospital after an episode of acute decompensation.[8] AKI is either prerenal, renal parenchymal, or obstructive in origin. AKI is associated with an increased risk of mortality because 2% to 31% of hospitalized cirrhotic patients with AKI do not survive their admission.[37,38] One- and 12-month mortality rates reported in these patients are 58% and 63%, respectively.[39] Even those who survive their hospital admission are more prone to complications of cirrhosis, including ascites and hepatic encephalopathy.[37,13]

DEFINITION AND CLASSIFICATION

KDIGO CRITERIA FOR AKI (2012):[40]

AKI is defined as any of the following (not graded):

- Increase in S. Creatinine by $\geq$ 0.3 mg/dl ($\geq$ 26.5 µmol/l) within 48 hours; or
- Increase in S. Creatinine to $\geq$ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume < 0.5 ml/kg/h for 6 hours.

STAGING OF AKI

Stage	Serum Creatinine	Urine Output
1	1.5 – 1.9 times baseline OR ≥ 0.3 mg/dl (≥ 26.5 µmol/l) increase	<0.5 ml/kg/h for 6-12 hours
2	2.0 – 2.9 times baseline	<0.5 ml/kg/h for ≥ 12 hours
3	3.0 times baseline OR Increase in serum creatinine to ≥ 4.0 mg/dl (≥ 353.6 µmol/l) OR Initiation of renal replacement therapy OR, In patients < 18 years, decrease in eGFR to <35 ml/min per 1.73 m^2	<0.3 ml/kg/h for ≥ 24 hours OR Anuria for ≥ 12 hours

The main modifications over the former, rather stringent criteria that were based on absolute serum creatinine level, was abandoning the arbitrary threshold of sCr> 1.5 mg/dl to diagnose AKI, since milder degrees of renal failure in patients with cirrhosis had often remained under diagnosed.[22] In addition, the use of urine output as part of the diagnostic criteria was eliminated, since many patients with cirrhosis and ascites maintain a preserved renal function despite being oliguric due to sodium and water retention.[41]

The spectrum of causes for AKI in cirrhosis includes:

i. Prerenal AKI (i.e. hypovolemia due to gastrointestinal bleeding, aggressive diuretic treatment, lactulose-induced diarrhea or infections).
ii. The hepatorenal syndrome-type AKI (HRS-AKI), which is defined as a potentially reversible deterioration of renal function unresponsive to volume resuscitation, caused by renal vasoconstriction in the absence of alternative identifiable causes. [42,43]

iii. Intrinsic causes such as acute tubular necrosis and, although very rare,
iv. Postrenal causes.

PRE-RENAL AKI

Patients with cirrhosis are predisposed to develop prerenal impairment due to underlying circulatory disturbances such as arterial underfilling (that occurs as a result of splanchnic vasodilation). Hypotension simultaneously reduces hepatic and renal perfusion and may dramatically compromise the functions of both the organs. The resulting changes in renal function include the excretion of small volume of concentrated sodium-deficient urine alongwith progressive azotemia.

These pathophysiological changes are mild in hypovolemia induced prerenal impairment, but severe in HRS, in which neurohormonal activation results in renal vasoconstriction and severely diminished renal perfusion. [44]

Pre renal AKI and HRS can be differentiated by the response to volume expansion. Hypovolemia-induced pre-renal impairment responds to volume expansion with rapid normalization of renal function, whereas HRS is insensitive to volume expansion, with no improvement in renal function.

In hypovolemia-induced pre-renal impairment, excessive fluid loss may be the result of various causes including vomiting, diarrhea, sodium and water restriction, gastrointestinal hemorrhage, large-volume paracentesis and excessive diuretic therapy.

Diarrhea may be a side effect of lactulose therapy in patients with hepatic encephalopathy.

Blood loss secondary to gastrointestinal haemorrhage is another cause of intravascular volume depletion, contributing to prerenalazotemia. The coagulopathy complicating advanced liver damage coupled with the upper gastrointestinal lesions commonly seen in cirrhotic patients makes gastrointestinal bleeding a common event.

Excess diuresis from overzealous use of diuretics is a common cause of intravascular volume contraction and prerenalazotemia. Diuretic

induced prerenal impairment occurs in 15% to 25% of patients with cirrhosis and ascites [45]. Impairment of distal sodium reabsorption increases the fractional excretion of the glomerular ultrafiltrate, thereby reducing plasma volume.

Nephrotoxic drugs, such as nonsteroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors and angiotensin II inhibitors, may precipitate prerenal failure by interfering with vasoactive mechanisms that modulate renal perfusion.

Infection is another significant cause of prerenal impairment and may precede septic shock. This precipitates renal impairment due to systemic vasodilation, arterial hypotension and diminished renal perfusion. Up to 10% of cases of SBP are associated with septic shock [46].

HRS type of AKI (HRS-AKI, formerly known as type 1 HRS)

The first consensus conference on a uniform definition for hepatorenal syndrome (HRS) took place in 1978 in Sassary, Italy.[47] HRS was then considered an acute renal dysfunction associated with extensive renal sodium water retention associated with acute or chronic liver disease. However, the evolving understanding of the pathophysiology of HRS has led to several reclassification and redefinitions.[42,47]

The traditional diagnostic criteria for acute renal failure in cirrhosis—a relative increase in serum creatinine (sCr) by 50% from baseline to a final value 1.5 mg/dL [26]—were replaced by the Acute Kidney Injury Network (AKIN) and Kidney Disease Improving Global Outcome (KDIGO) diagnostic criteria for AKI [48,40] and specifically adapted for patients with cirrhosis in order to improve applicability into clinical practice (ICA criteria) [41]. The most recent definition criteria were published in 2015 by both a community of hepatologists (ICA) together with the Acute Dialysis Quality Initiative (ADQI), a community of nephrologists, and reclassified the former type 1 HRS as a special entity of acute kidney injury: the ‘HRS type of AKI’ (HRS-AKI) [41].

Diagnostic criteria of hepatorenal syndrome (HRS) type of acute kidney injury (AKI) in patients with cirrhosis HRS-AKI [41]

- Diagnosis of cirrhosis and ascites
- Diagnosis of AKI according to ICA-AKI criteria
- No response after 2 consecutive days of diuretic withdrawal and plasma volume expansion with albumin 1 g per kg of body weight
- Absence of shock
- No current or recent use of nephrotoxic drugs (NSAIDs, aminoglycosides, iodinated contrast media, etc.)
- No macroscopic signs of structural kidney injury*, defined as:
  - absence of proteinuria (>500 mg/day)
  - absence of microhaematuria (>50 RBCs per high power field),
  - normal findings on renal ultrasonography

*Patients who fulfil these criteria may still have structural damage such as tubular damage. Urine biomarkers will become an important element in making a more accurate differential diagnosis between HRS and acute tubular necrosis.

[ICA,International Club of Ascites; NSAIDs, non-steroidal anti-inflammatory drugs; RBCs, red blood cells.]

International Club of Ascites (ICA-AKI) new definitions for the diagnosis and management of AKI in patients with cirrhosis [41]

Definition of AKI -

- Increase in sCr ≥0.3 mg/dl (≥26.5 μmol/L) within 48 hours; or,
- A percentage increase sCr ≥50% from baseline which is known, or presumed, to have occurred within the prior 7 days

In the past two decades, two different types of HRS have been distinguished. While type 1 HRS describes a fulminant decline in renal function in patients with advanced liver disease that is associated with a detrimental prognosis (occurs over 2 weeks and has high mortality), type 2 HRS is defined as slowly progressive functional renal failure that typically occurs in patients with refractory ascites (occurs over a much longer period of time and has less mortality). [49]

Apart from the time of development, the same specific diagnostic criteria for HRS-AKI also apply for HRS type 2.[26] In general, prognosis

in HRS type 2 is poor, but more favourable when compared to AKI-HRS.[39]

Difference between HRS Type I and HRS Type II[49]

HRS Type I	HRS Type II
Rapidly progressive	Slower deterioration
Serum creatinine double to >2.5 mg/dL or creatinine clearance <20 mL/min in <2 weeks	Serum creatinine >1.5 mg/dL or creatinine clearance <40 mL/min but decline is slow
Prognosis—80% die in 2 weeks	Most patients die within several weeks
Frequently precipitating events (e.g. spontaneous bacterial peritonitis)	Most frequent cause of therapy-resistant ascites

Pathophysiology of the hepatorenal syndrome

The understanding of the various pathophysiological pathomechanisms of renal dysfunction in cirrhosis has drastically evolved over the past few years and decades.

HRS-AKI—the 'classical vasodilation theory'

The development of HRS-AKI is supposedly caused by intrarenal vasoconstriction due to circulatory dysfunction in decompensated cirrhosis. Indeed, the pathophysiology of HRS is closely linked to the development of ascites, which is considered a prerequisite for the development of HRS [47,50,51]. In 1988, Schrier and colleagues proposed the peripheral arterial vasodilation hypothesis for ascites [52,53]. According to this hypothesis, due to structural changes in the fibrotic tissue, intrahepatic vascular resistance is increased, causing portal hypertension and an over expression of compensatory vasodilating factors [54]. The vasodilating factors accumulate in the splanchnic area and, in later stages, in the systemic circulation [55,56]. This causes a pooling effect in the splanchnic vessels, leading to increased shear-

wall stress and transudation of plasma into the abdominal cavity: ascites [57]. As a consequence, effective circulating blood volume and mean arterial pressure are decreased. This activates the sympathetic nervous system, initiating a hyperdynamic circulation, but also stimulating the renin-angiotensin-aldosterone system (RAAS) [58]. Excessive RAAS activation promotes water and sodium retention, thereby aggravating ascites formation via aldosterone and high levels of angiotensin II induce renal vasoconstriction.[59] In situations of hemodynamic stress such as in case of volume loss (e.g. due to diuretics, dehydration or gastrointestinal bleeding) or bacterial infections, RAAS activation and circulatory dysfunction may reach a point at which renal function can no longer be maintained—and HRS-AKI ensues [6].

HRS-AKI as part of a multiorgan failure syndrome/systemic inflammatory response syndrome (SIRS) - a new hypothesis

There is increasing evidence that systemic inflammation also plays an important role in the development of complications of portal hypertension in cirrhosis[60]. Until 2007, sepsis was an exclusion criterion for HRS[47]. However, in cirrhosis, renal dysfunction often develops secondarily to bacterial infections. SIRS and sepsis supposedly lead to renal blood flow redistribution, resulting in ischemia and subsequent tubular injury [61,62].

Toll-like receptor 4 (TLR4) is the main pattern-recognition receptor in the detection of inflammatory signals that has been identified to play an important role in the development of HRSAKI in experimental models of cirrhosis. TLR4 is over expressed in kidney tissue and urine in patients with cirrhosis and AKI (including HRS-AKI patients) following an inflammatory insult [63,64]. Endotoxins or lipopolysaccharides (LPS) are particles of the cell wall of Gram-negative bacteria and represent natural ligands to TLR4. LPS are strong pro-inflammatory factors by inducing TNF-a [65]. In cirrhosis, high levels of LPS (e.g. in case of spontaneous bacterial peritonitis [SBP] or sepsis) increase portal pressure and may induce hepatocyte death—thereby promoting hepatic decompensation[66–68]. This may eventually lead to deterioration

of the systemic circulation, shock and multiorgan failure, including (HRS-) AKI. Indeed, SBP and sepsis represent the most common precipitating events for HRS-AKI. Recent studies on terlipressin for treatment of HRS-AKI showed similar outcomes of patients with sepsis- and SIRS-induced HRS-AKI treated with terlipressin, which indicates similarities in pathophysiology between patients with and without infections as triggers[69–71].

Besides cirrhosis, HRS-like AKI may also develop in acute settings, (i.e. acute or acute-on-chronic liver failure or steatohepatitis) due to excess liberation of pro-inflammatory cytokines or chemokines. These acute situations may also induce renal tubular damage due to upregulation of inflammatory mediators, chemokines and cytokines that may directly cause renal damage and further induce circulatory dysfunction and worsening of systemic vasodilatation (Acute tubular necrosis, ATN). As a result, in contrast to HRS-AKI as functional renal failure, ATN may not respond to vasoconstrictor therapy [69].

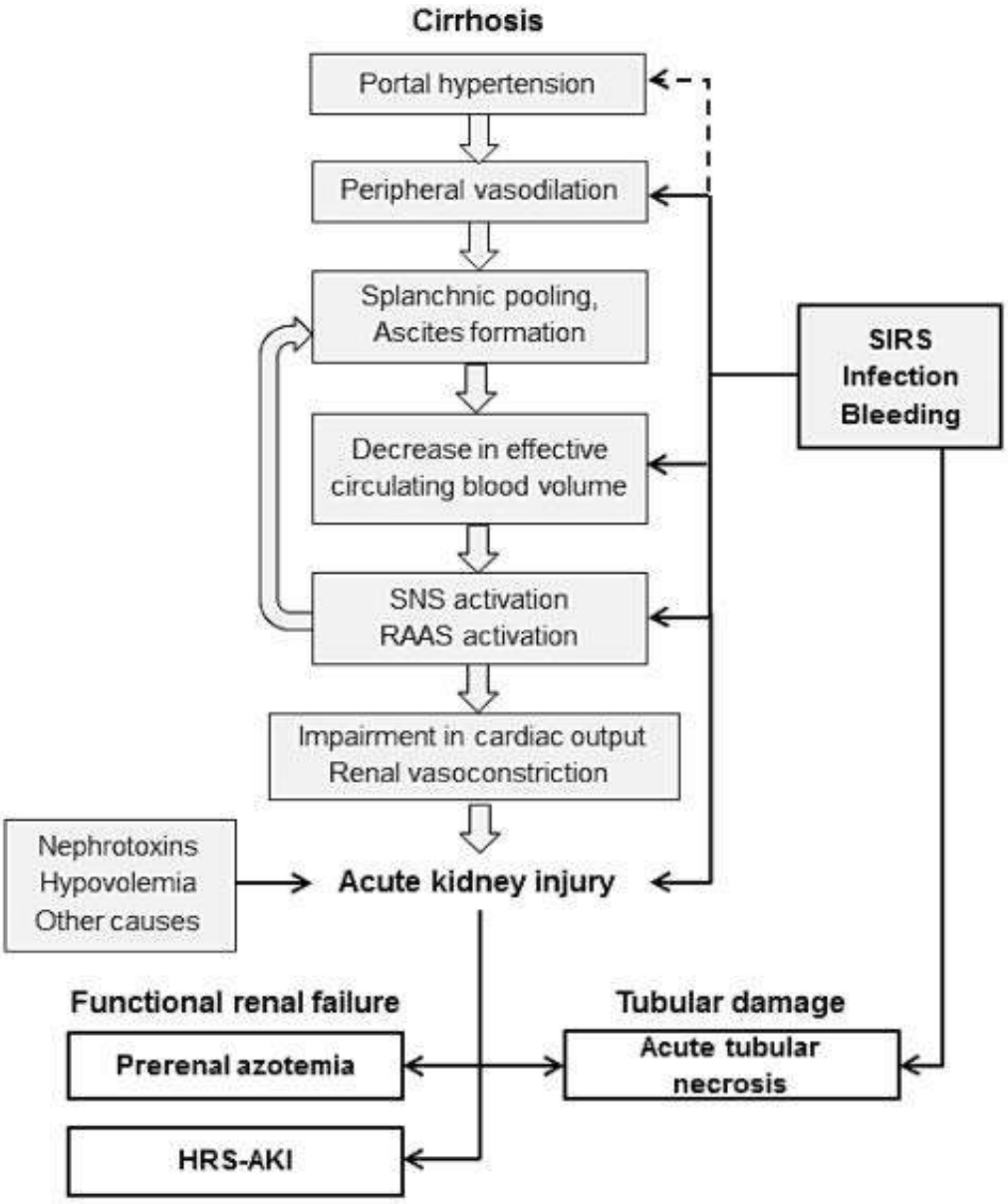


Figure showing Pathophysiology of acute kidney injury (AKI) and hepatorenal syndrome (HRS) in decompensated cirrhosis. Broad arrows: vasodilation theory of ascites formation. Black arrows: 'inflammation theory' and further aspects of AKI development. Dashed line: impact of infections (i.e. spontaneous bacterial peritonitis) on portal hypertension. SNS, sympathetic nervous system; RAAS, renin-angiotensin-aldosterone system; SIRS, systemic inflammatory response syndrome; HRS-AKI, hepatorenal syndrome type of acute kidney injury[26,42,47,48]

Structural changes in HRS-AKI

There is increasing evidence for structural renal changes at least in a subgroup of patients with end-stage liver diseases. Patients with cirrhosis and impaired renal function were reported to show glomerular, vascular and tubulo-interstitial pathologies even in the absence of proteinuria and hematuria [72,73]. Patients with cirrhosis might suffer from specific renal pathologies associated with liver diseases such as IgA nephropathy in alcoholic cirrhosis or cryoglobulinemia in hepatitis C or other, non-cirrhosis-specific nephropathies (e.g. diabetic nephropathy).

The evidence that renal dysfunction in HRS is functional is substantial [74]. Reversal of the renal dysfunction with HRS occurs with liver transplantation in spite of the nephrotoxic effects of immunosuppressive drugs, e.g. calcineurin inhibitors. Renal parenchymal histology in HRS has been shown to be virtually normal, thus not providing an explanation for GFRs <30 mL/min/1.73m2 in HRS. Furthermore, there is now evidence for reversal of HRS by treating the arterial underfilling, which occurs secondary to splanchnic vasodilatation. This approach to reverse HRS, other than liver transplantation, involves the combination of terlipressin (V1 AVP agonist) and albumin [75].

INTRINSIC AKI

Intrinsic renal impairment may be caused by abnormalities in -

- renal tubules (eg, ATN),
- glomeruli (eg, glomerulonephritis) or
- interstitium (eg, interstitial nephritis).

It should be suspected in patients with proteinuria (>500 mg/dL [>5 g/L]) and/or hematuria (>50 red cells per high-powered field). A careful review of the medical history, including comorbidities and drug history, is often helpful in achieving the correct diagnosis. Renal biopsy is reserved for indeterminate cases in which obtaining histological diagnosis may alter patient management or prognosis.[31]

ACUTE TUBULAR NECROSIS: ATN is the most common cause of intrinsic renal impairment in patients with cirrhosis. According to separate reports, ATN accounts for <32%, 41.7% and 44.4% of cases of renal impairment in cirrhosis[11,76,77]. ATN may be either ischemic or toxic, while the clinical course is divided into initiation (hours to weeks), maintenance (one to two weeks) and recovery stages.

Hypovolemia-induced prerenal impairment may progress into ischemic ATN in severe cases. Aminoglycoside antibiotics are the most common cause of toxic ATN, and others include nonsteroidal anti-inflammatory drugs, calcineurin inhibitor immunosuppression and radioiodine contrast agents. While radioiodine contrast agents are safe in patients with normal renal function, those with borderline renal function are at an increased risk for nephrotoxicity.

In a prospective study involving 404 patients with cirrhosis, Prakash et al[77] found that precipitating factors for ATN included sepsis (most commonly SBP followed by urinary tract infection) in 61.4%, hypovolemia (most commonly gastrointestinal bleed followed by septic shock) in 36.4% and nephrotoxic drugs in 2.3%.

In ATN, the tubular ability to reabsorb sodium and concentrate urine is impaired, leading to high urinary sodium (> 40 mEq/L), high fractional excretion of sodium (2%) and low urinary osmolality (<350mOsm/kg) [11]. Conversely, patients with HRS have low urinary sodium (<20 mEq/L), low fractional excretion of sodium (<1%) and elevated urinary osmolality (>500 mOsm/kg) [11]. Nevertheless, differentiation can be challenging in patients with cirrhosis because diuretic therapy can lead to a urinary sodium >10 mEq/L while a fractional sodium excretion ≤1% is occasionally found in ATN[11]. Granular casts may be found in both ATN and HRS, but epithelial casts favour ATN [11,74].

GLOMERULONEPHRITIS: Chronic HBV and HCV cirrhosis are associated with a variety of glomerular diseases such as membrano proliferative glomerulonephritis (most common glomerular disease induced by HCV) with or without cryoglobulinemia, membranous nephropathy (most common glomerular disease induced by HBV) and focal glomerulosclerosis[78,79].

Abnormalities of immunoglobuilin (Ig)A have been reported in patients with alcohol-related cirrhosis, including mesangial IgA deposits and development of secondary IgA nephropathy[80,81]. Elevated circulating serum IgA is common in patients with alcohol related liver disease, while mesangial IgA renal deposits are reported at autopsy in 36% of those with cirrhosis [82,83].

INTERSTITIAL NEPHRITIS: Interstitial nephritis is most commonly due to drug-induced hypersensitivity reactions.

POST RENAL AKI

Postrenal impairment due to urinary tract obstruction is an uncommon cause of renal dysfunction, accounting for <1% of AKI cases in cirrhosis[11]. The presence of hydronephrosis on imaging differentiates postrenal from prerenal or intrinsic renal causes of kidney dysfunction.

Urinary tract obstruction has many causes. In a retrospective study of 888 patients admitted to intensive care from 1998 to 2010, Hamdi et al [84] found that malignancy represented one-half of all causes of postrenal AKI. Prostate cancer was the most common malignancy (55%) while pelvic cancers as a group accounted for 90% of all malignancies. Other causes of postrenal impairment include benign prostatic hypertrophy (21%), urinary tract calculi (10%) and, less often, retroperitoneal fibrosis, urethral stricture, postradiationureteritis, bladder dysfunction and papillary necrosis.

However, certain causes of obstructive uropathy occur with increased frequency in patients with advanced liver disease. Papillary necrosis is said to occur more frequently in patients with alcoholic liver disease than in the general population [85].

The bleeding diathesis caused by failure of the damaged liver to synthesize coagulation factors normally may result in hematuria and the excretion of clots. The formation of large clots in the collecting system can prevent free passage of urine, creating postrenal AKI in the cirrhotic patient. Retroperitoneal haemorrhage can complicate any coagulopathy. Bleeding in this area provokes a desmoplastic reaction that causes the ureters to become enveloped in fibrous tissue. Although the lumen of a ureter embedded in this scar tissue is patent,

the fibrosis prevents transmission of peristaltic waves, thereby creating a functional block of urine flow [86].

Resolution of acute urinary tract obstruction may be associated with post obstructive diuresis as defined by a urine output >4 L per day. Close monitoring is required during this stage because excessive urinary losses can lead to hypovolemia and electrolyte disturbance.[84]

BIOMARKERS IN AKI

Early treatment of AKI is crucial for determining outcome, and therefore it is important to ascertain the type of AKI. Serum creatinine concentration has been used to diagnose and assess the severity of AKI in routine clinical practice. However, serum creatinine is determined not only by renal function, but also by dietary protein intake, muscle mass and activity, and nonrenal clearance.[87]

Cirrhotic patients have a chronic disease with loss of muscle mass that affects the relationship between serum creatinine and GFR. Unpublished results demonstrated in 318 cirrhotic patients that a serum creatinine of 1.3 mg/Dl equated to a mean GFR of 48 mL/min/1.73m2, while a serum creatinine of 2.0 mg/dL equaled to 20 mL/min/ 1.73m2. Thus, the relationship between GFR and serum creatinine in a cachectic patient with advanced cirrhosis needs to be considered. In this setting, ‘normal’ serum creatinine (<1.5 mg/dL) may still indicate substantial renal dysfunction.[49]

Moreover, most patients with advanced decompensated cirrhosis have ascites and fluid overload, which also affects the accurate measurement of serum creatinine concentration.[88] High bilirubin levels also may affect the accuracy of serum creatinine in plasma samples owing to spectral effects and reacting with the assay reagents, leading to a lowering of the laboratory-reported serum creatinine concentration.[89]

A fractional excretion of urinary sodium (FENa) of less than 1% has been widely used to differentiate patients with prerenal AKI, but patients with HRS AKI also may have reduced FENa. Although it has been suggested that a very low FENa of <0.1% may be supportive of a diagnosis of prerenal AKI in patients with cirrhosis, it must be

remembered that not only does the ability to concentrate urinary sodium fall with age, but that urinary sodium excretion also can be affected by diuretics and sepsis [90].

Urinary biomarkers have the potential for being more sensitive than serum creatinine in cirrhosis. Fagundes et al. [91] have reported in abstract form that fractional excretion of sodium, is significantly higher in patients with ATN than HRS. Such results further support the functional nature of HRS compared to ATN in cirrhotic patients.

MATERIALS AND METHODS

This study included 100 consecutive patients of age ≥ 18 years admitted in Dayanand Medical College and Hospital, Ludhiana with liver cirrhosis and are were found to have acute renal dysfunction.

SOURCE OF DATA:

This study included 100 consecutive patients of liver cirrhosis admitted in the Department of Medicine and Allied Super specialities in Dayanand Medical College and Hospital, Ludhiana who were found to have acute renal dysfunction on admission.

METHOD OF COLLECTION OF DATA

All the patients included in this study were assessed as follows-

1-Clinical assessment

Detailed history of presenting complaints were taken.

Relevant past, personal, drug history and family history was taken

Findings of general and systemic findings were recorded.

2- Laboratory investigations

The results of routine investigations like CBC, RFT, LFT, RBS, Urine routine, CXR, ECG were recorded in all cases.

The results of PTI/INR, ESR, Arterial Ammonia, USG Abdomen, Ascitic fluid analysis, relevant C/S, viral markers were also recorded. The results of urinary protein to creatinine ratio, spot urinary sodium, and other investigations for renal dysfunction were recorded.

Investigations like ABG, Upper GI Endosopy, Fibroscanwere optional and done wherever indicated.

INCLUSION CRITERIA – Presence of all of the following –

- Age ≥ 18 years
- Those who gave consent
- Diagnosed cases of cirrhosis based on history, examination, LFTs, USG Abdomen & Fibroscan (wherever indicated).
- Renal dysfunction suggestive of AKI as per KDIGO criteria (2012).

EXCLUSION CRITERIA –

- Pregnant females
- Patients of chronic renal failure were excluded based on history, examination and USG showing small kidneys.
- Patients of liver cirrhosis having renal involvement previously enrolled in this study and were readmitted were excluded.

OUTCOME: The outcome was recorded as under-

a) Outcome of the patient at the end of hospital stay – Discharged/ Death

b) Recovery of renal dysfunction at the end of hospital stay – Not recovered/ partially recovered/ completely recovered.

STATISTICAL ANALYSIS

Data was described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

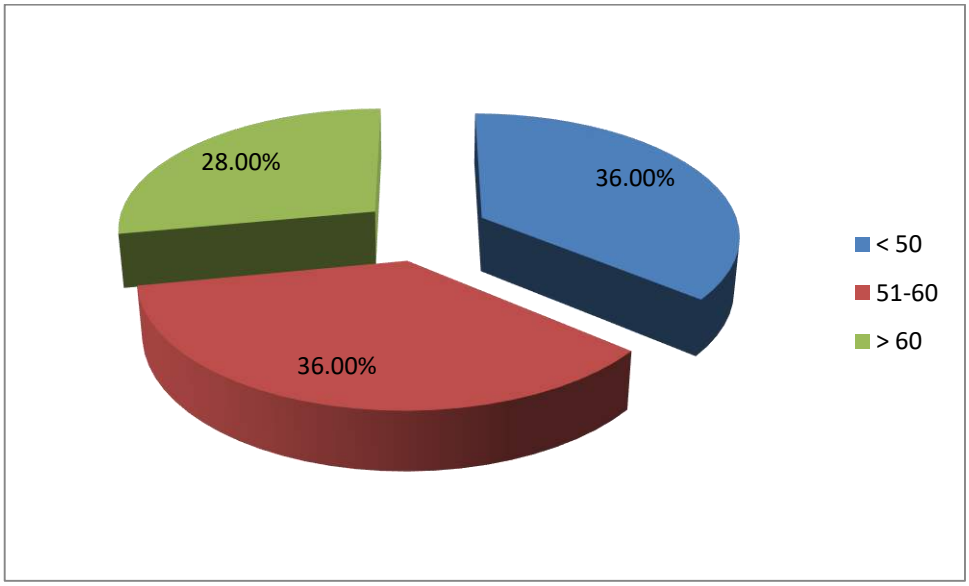
OBSERVATIONS AND RESULTS

The study incorporated 100 consecutive patients of age ≥ 18 years with liver cirrhosis which were screened for acute renal dysfunction.

Table 1 - Age Wise Distribution of the Patients

Age group	No. of cases	Percentage
< 50	36	36.0%
51-60	36	36.0%
> 60	28	28.0%
Total	100	100.0%

Figure 1 - Age Wise Distribution of the Patients

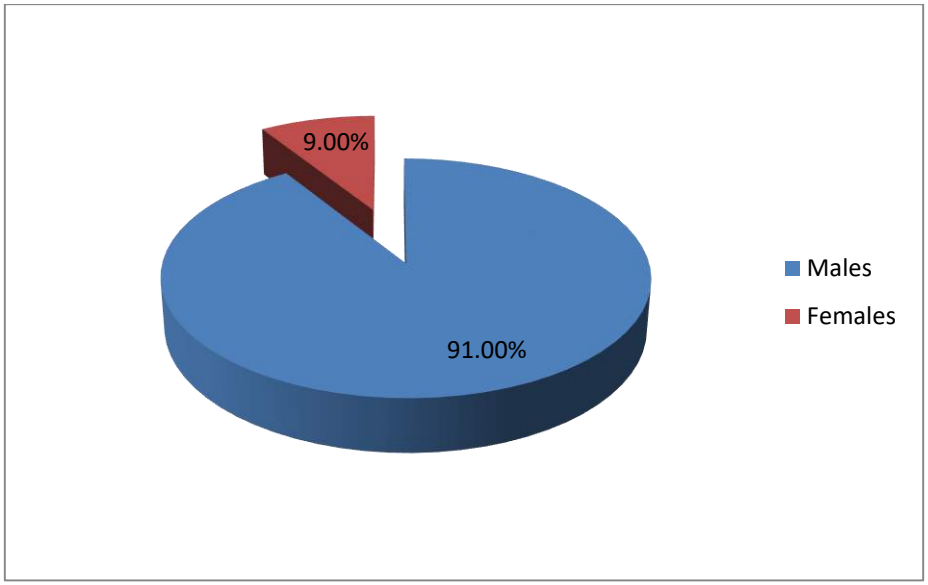


The mean age of the patients in our study was 52.60 ± 10.89 years with the minimum being 29 years and maximum being 75 years. Majority of the patients were more than 50 years of age (64%).

Table 2 – Sex Wise Distribution of the Patients

Sex	No. of cases	Percentage
Males	91	91.0%
Females	9	9.0%
Total	100	100.0%

Figure 2 – Sex Wise Distribution of the Patients

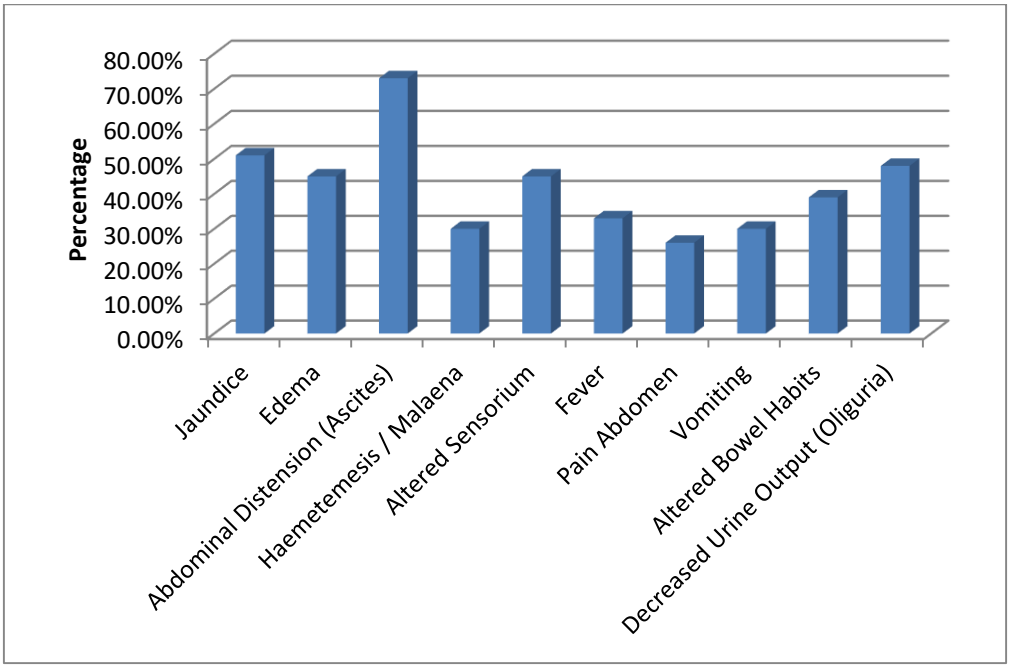


Our study population had male preponderance - males (91%) & females (9%).

Table 3 - Presenting Complaints of the Patients

Presenting Complaints	No. of cases	Percentage
Jaundice	51	51.0%
Edema	45	45.0%
Abdominal Distension (Ascites)	73	73.0%
Haemetemesis / Malaena	30	30.0%
Altered Sensorium	45	45.0%
Fever	33	33.0%
Pain Abdomen	26	26.0%
Vomiting	30	30.0%
Altered Bowel Habits	39	39.0%
Decreased Urine Output (Oliguria)	48	48.0%

Figure 3 - Presenting Complaints of the Patients

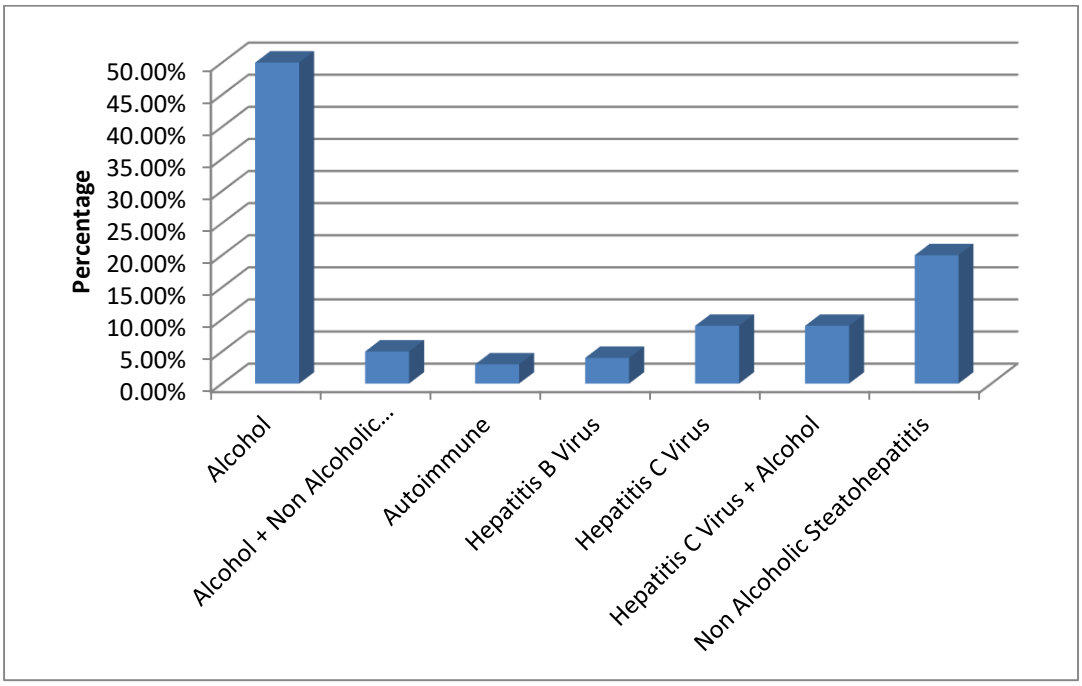


The most common symptom in our study was decreased urine output seen in 100% of the patients, next common reported symptom was abdominal distension (73 %), followed by jaundice (51 %), pedal edema (45%) and altered sensorium (45%). Haemetemesis/Malaena, fever, pain abdomen, vomiting, altered bowel habits were seen in about 26% to 39% of the patients.

Table 4- Distribution of Patients according to Etiology of Cirrhosis

Etiology of Cirrhosis	No. of cases	Percentage
Alcohol	50	50.0%
Alcohol + Non Alcoholic Steatohepatitis	5	5.0%
Autoimmune	3	3.0%
Hepatitis B Virus	4	4.0%
Hepatitis C Virus	9	9.0%
Hepatitis C Virus + Alcohol	9	9.0%
Non Alcoholic Steatohepatitis	20	20.0%
Total	100	100.0%

Figure 4- Distribution of Patients according to Etiology of Cirrhosis

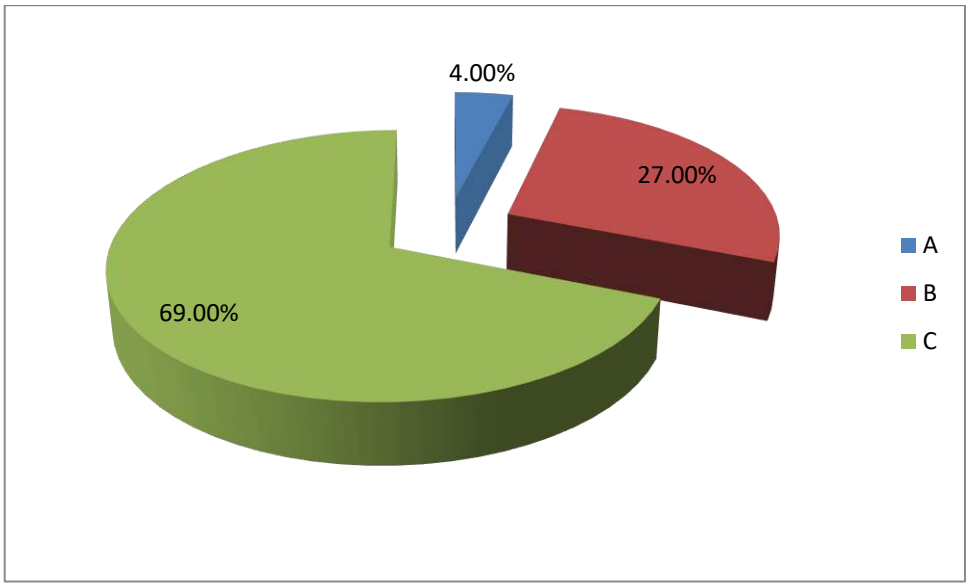


Half of the study patients had alcohol related cirrhosis (50%). Non Alcoholic Steatohepatitis was the etiology of cirrhosis in 20% of the patients. Hepatitis B and C virus related cirrhosis was noted in 13% of the patients. More than one etiology of cirrhosis was seen in 14% of patients of which most common was combined Hepatitis C virus and alcohol related cirrhosis, seen in 9% of patients.

Table 5 - Distribution of Patients according to CTP Class

CTP CLASS	No. of cases	Percentage
A	4	4.0%
B	27	27.0%
C	69	69.0%
Total	100	100.0%

Figure 5 - Distribution of Patients according to CTP Class

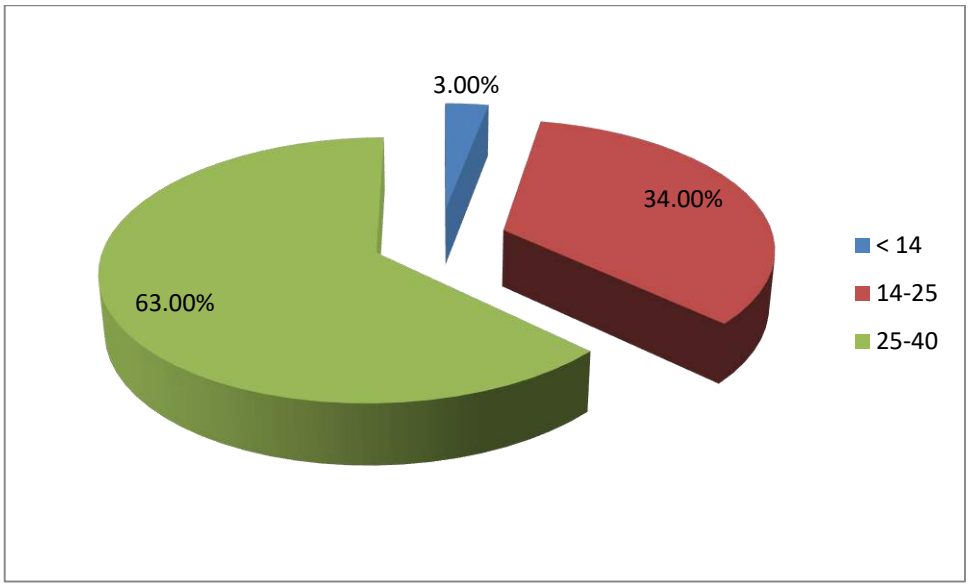


In the study population; 4, 27 and 69 patients had Child A, B and C cirrhosis respectively on admission. Majority of the patients in the study (i.e.69%) had CTP Grade C.

Table 6 - Distribution of Patients according to MELD Score

MELD Score	No. of cases	Percentage
< 14	3.0	3.0%
14-25	34.0	34.0%
25-40	63.0	63.0%
Total	100	100.0%

Figure 6 - Distribution of Patients according to MELD Score

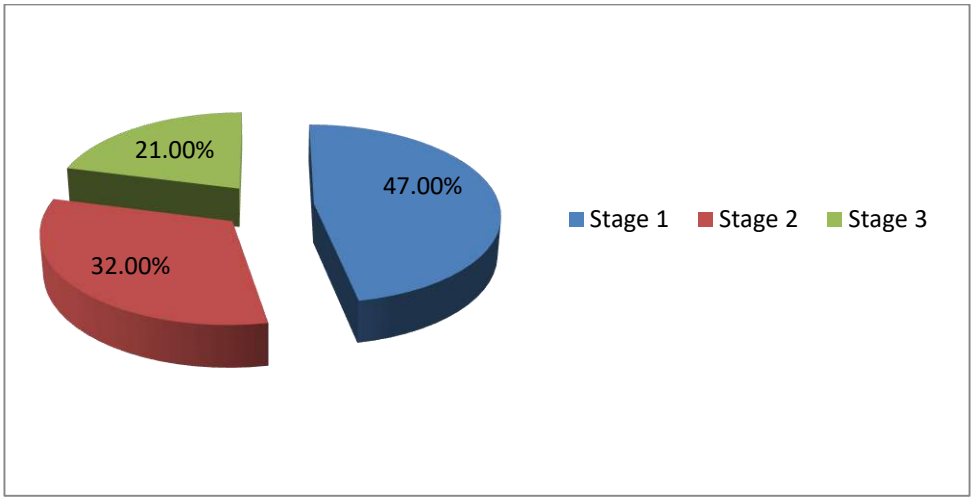


The mean MELD score was 27.95 ± 7.89, with 97% patients having a MELD score ≥ 14; minimum MELD Score being 11 and maximum being 40.

Table 7 –Distribution of Patients according to Stage of AKI (as per KDIGO Guidelines 2012)

Stage	S. Creatinine	No. of cases	Percentage
1	1.5–1.9 times baseline OR ≥ 0.3 mg/dl increase	47.0	47.0%
2	2.0–2.9 times baseline	32.0	32.0%
3	3.0 times baseline OR Increase in serum creatinine to ≥ 4.0 mg/dl OR Initiation of renal replacement therapy	21.0	21.0%

Figure 7 –Distribution of Patients according to Stage of AKI (as per KDIGO Guidelines 2012)

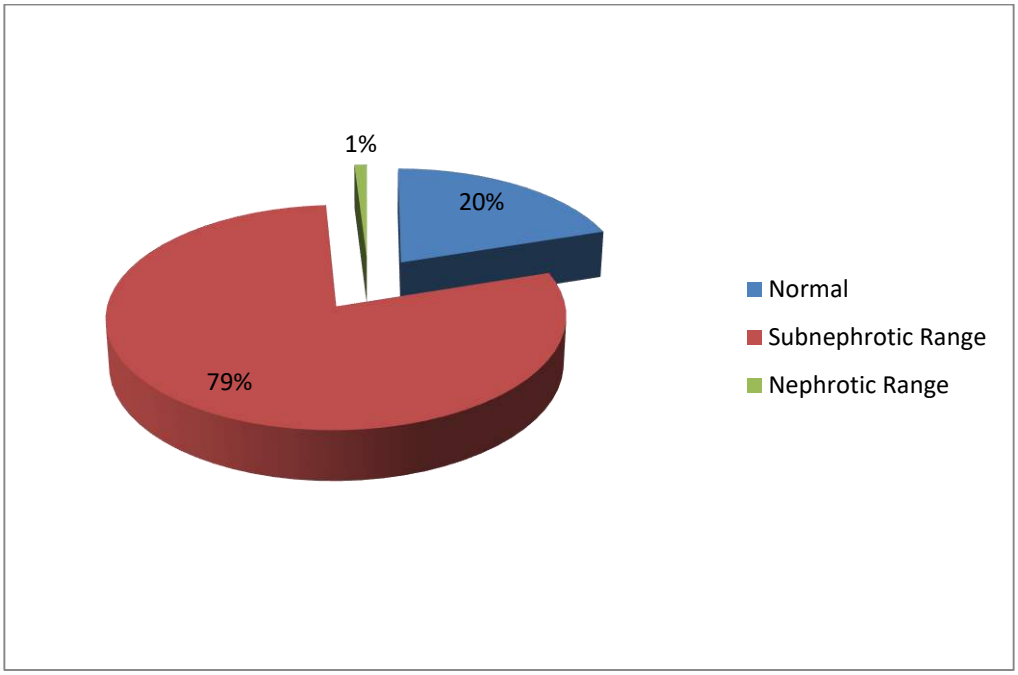


At the time of presentation 47% patients had stage 1 AKI, 32% patients had stage 2 AKI and 21% patients had stage 3 AKI.

Table 8 – Distribution of Patients according to Range of Proteinuria

	UPCR	No. Of cases	Percentage
Normal	<0.15	20	20%
Subnephrotic Range	0.15-3.5	79	79%
Nephrotic Range	>3.5	1	1%

Figure 8 – Distribution of Patients according to Range of Proteinuria

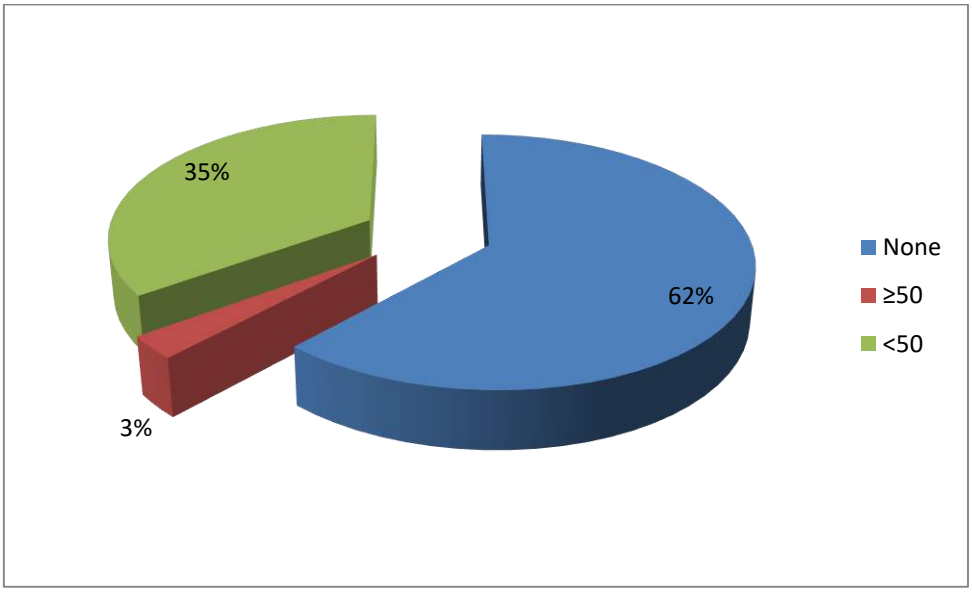


Maximum number of cases in our study had subnephrotic range proteinuria (79% cases) whereas nephrotic range proteinuria was seen in only 1% cases.

Table 9 – Distribution of Patients according to amount of Hematuria

RBC/HPF	No. Of cases	Percentage
None	62	62%
≥50	3	3%
<50	35	35%

Figure 9 – Distribution of Patients according to amount of Hematuria

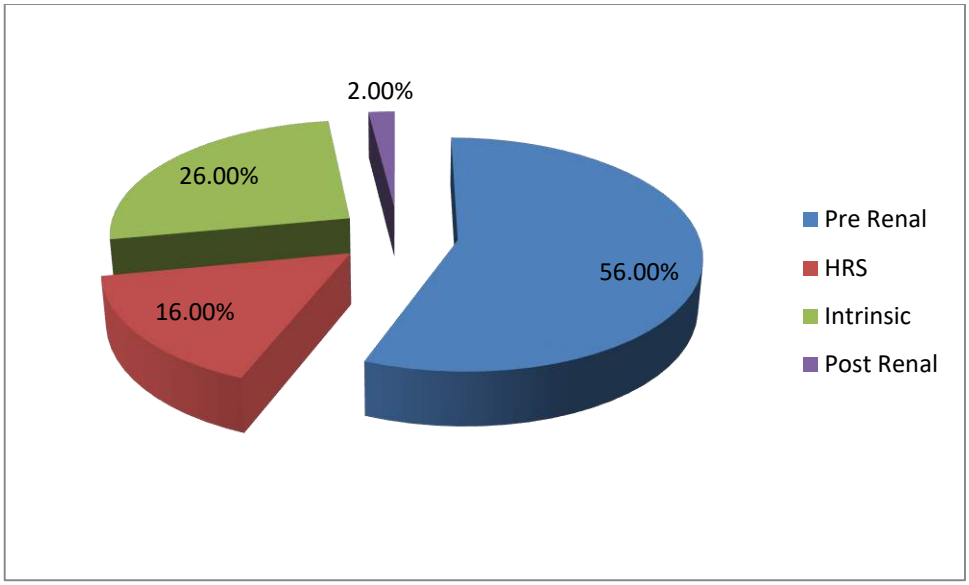


Majority of cases in our study (62%) had no hematuria, 3% had ≥ 50 RBC/HPF whereas 35% had < 50 RBC/HPF.

Table 10 – Distribution of Patients according toType of Acute Kidney Injury

Type of Acute Kidney Injury	No. of cases	Percentage
Pre Renal	56	56.0%
HRS	16	16.0%
Intrinsic	26	26.0%
Post Renal	2	2.0%
Total	100	100.0%

Figure 10 – Distribution of Patients according toType of Acute Kidney Injury

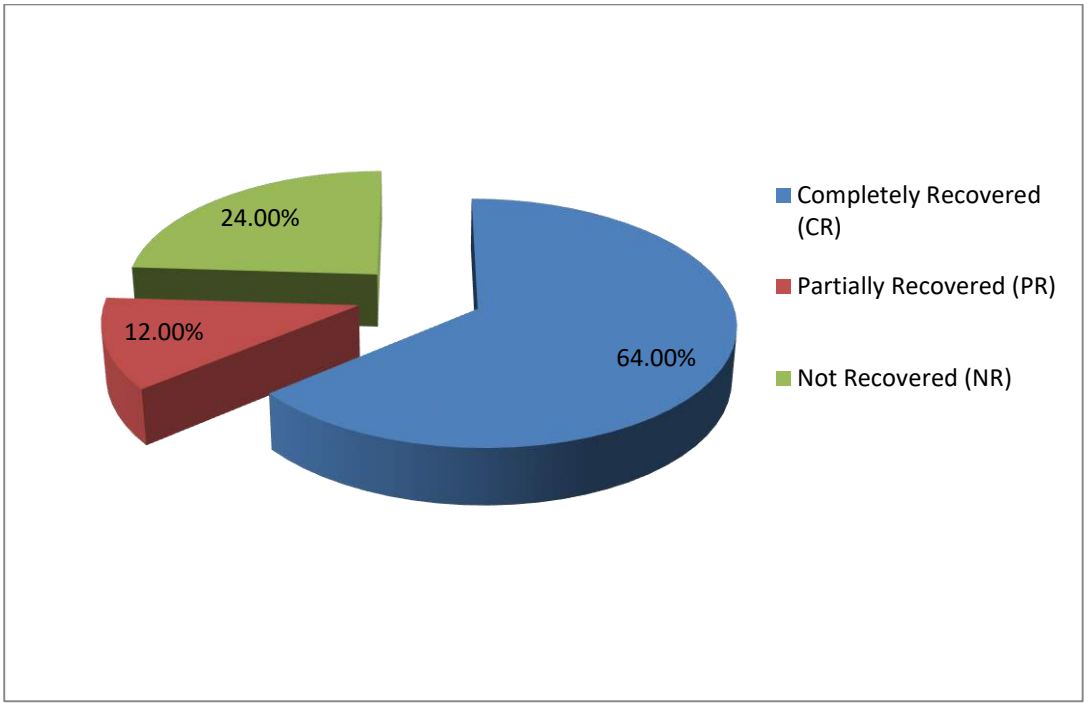


The most common type of acute kidney injury observed in our study was Pre- renal (56%), followed by Intrinsic (26%), HRS (16%), post renal type of renal dysfunction was seen in only 2% of the patients.

Table 11 – Distribution of Patients according toRecovery of Acute Kidney Injury at end of hospital stay

Recovery of Acute Kidney Injury	No. of cases	Percentage
Completely Recovered (CR)	64	64.0%
Partially Recovered (PR)	12	12.0%
Not Recovered (NR)	24	24.0%
Total	100	100.0%

Figure 11 – Distribution of Patients according toRecovery of Acute Kidney Injury at end of hospital stay

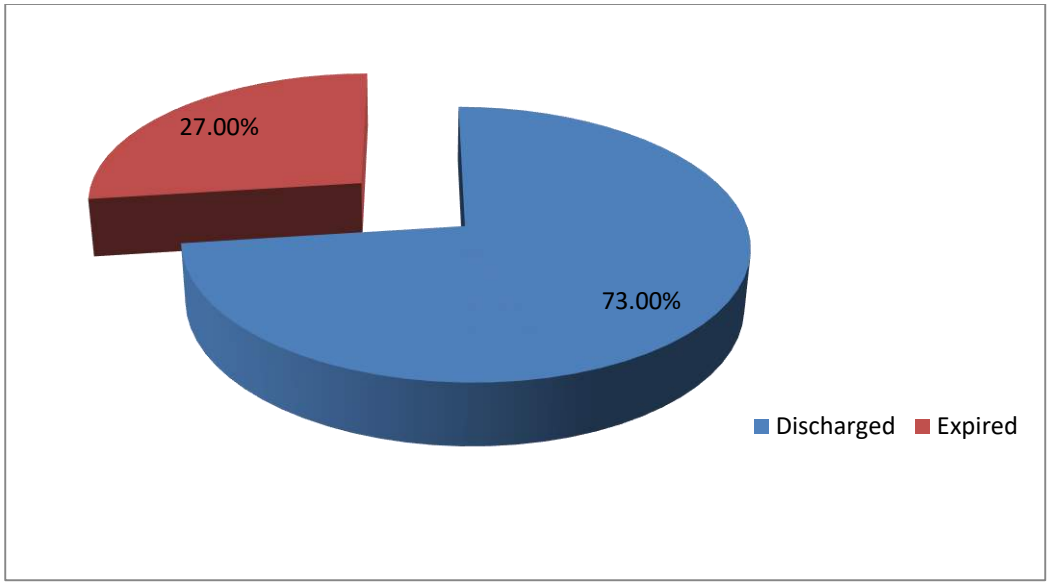


Acute kidney injury recovered completely in majority of patients i.e 64%, recovered partially in 12 % of the patients. Acute kidney injury did not recover in 24% of the patients.

Table 12 – Distribution of Patients according to Mortality Outcome at the end of hospital stay

	No. of cases	Percentage
Discharged/ Alive	73	73.0%
Expired	27	27.0%
Total	100	100.0%

Figure 12 – Distribution of Patients according to Mortality Outcome at the end of hospital stay



The mortality rate was found to be approximately 27% and a survival rate of 73%. The patients who left against medical advise were terminal and with a very poor prognosis and hence were included among non-survivors.

BASELINEINVESTIGATIONS OF THE STUDY POPULATION AT TIME OF ADMISSION

Table 13 – Mean Values of Baseline Hepatic Parameters of the study population

	No. Of Patients	**Mean**	**Std. Deviation**	**Minimum**	**Maximum**
Total Bilirubin (mg/dl)	100	9.03	9.94	0.61	42.77
SGOT (U/L)	100	124.40	129.28	21.00	800.00
SGPT (U/L)	100	84.64	158.61	7.00	1058.00
ALP (U/L)	100	169.48	139.12	41.00	972.00
S. Albumin (g/dl)	100	2.61	0.55	1.36	3.90
PTI (sec)	100	22.08	9.16	11.80	61.40
INR	100	2.03	0.88	1.08	6.00
Ammonia (umol/L)	71	136.63	82.70	27.00	488.00
SAAG (g/dl)	77	1.95	0.48	1.03	3.30
CTP SCORE	100	10.57	2.20	6.00	15.00
MELD	100	27.95	7.89	11.00	40.00

Mean value of total bilirubin was 9.03 $\pm$ 9.94 mg/dl. Mean values for SGOT and SGPT were 124.40 $\pm$ 129.28 U/L and 84.64 $\pm$ 158.61 U/L respectively. Mean serum albumin was 2.61 $\pm$ 0.55 g/dl.

Mean values of PTI/INR were 22.08 + 9.16 sec and 2.03 + 0.88 respectively.

Ammonia levels were seen in only 71 patients, in which the mean value was 136.63 $\pm$ 82.70 umol/L.

Ascitic fluid analysis was done in only 77 patients and the mean value of SAAG was found to be 1.95 $\pm$ 0.48 g/dl.

Mean CTP Score was 10.57 $\pm$ 2.20. Mean MELD Score was 27.95 $\pm$ 7.89.

Table 14 – Mean values of Baseline Renal Parameters of the study population

	No. of Patients	**Mean**	**Std. Deviation**	**Minimum**	**Maximum**
S. Urea (mg/dl)	100	90.97	55.46	16.00	271.00
S.Creatinine (Day 1) (mg/dl)	100	2.40	1.45	1.22	10.21
S.Creatinine (Day 3) (mg/dl)	100	2.32	1.80	0.50	11.40
S. Sodium (mmol/L)	100	132.29	7.42	106.00	150.00
S. Potassium (mmol/L)	100	4.53	0.96	2.35	7.53
Spot urine protein creatinine ratio	100	0.52	0.62	0.07	5.10
Estimated Creatinine Clearance (ml/min)	100	44.83	22.03	10.00	106.00
Spot Urinary Sodium (mmol/L)	100	29.77	22.26	5.00	127.00
Fractional Excretion of Sodium (%)	100	0.92	1.92	0.00	17.40

Mean values of blood urea on admission was 90.97 $\pm$ 55.46 mg/dl. Mean values for S.Creatinine on day 1 of admission and day 3 i.e. 48 hours apart were 2.40 $\pm$ 1.45 mg/dl and 2.32 $\pm$ 1.80 mg/dl respectively. Mean serum albumin was 2.61 $\pm$ 0.55 g/dl.

Mean value of UPCR was 0.52 $\pm$ 0.62. Mean creatinine clearance was 44.83 $\pm$ 22.03. Mean urinary spot sodium was 29.77 $\pm$ 22.26 mmol/L

Mean value of FENa was 0.92 + 1.92 %.

Table 15 – Mean values of Baseline Haematological Parameters of the study population

	No. Of Patients	**Mean**	**Std. Deviation**	**Minimum**	**Maximum**
Haemoglobin (gm/dl)	100	9.42	2.43	3.30	14.70
TLC (10^3/ul)	100	13.80	8.03	2.20	40.20
Platelets (10^3/ul)	100	122.85	70.41	22.00	408.00

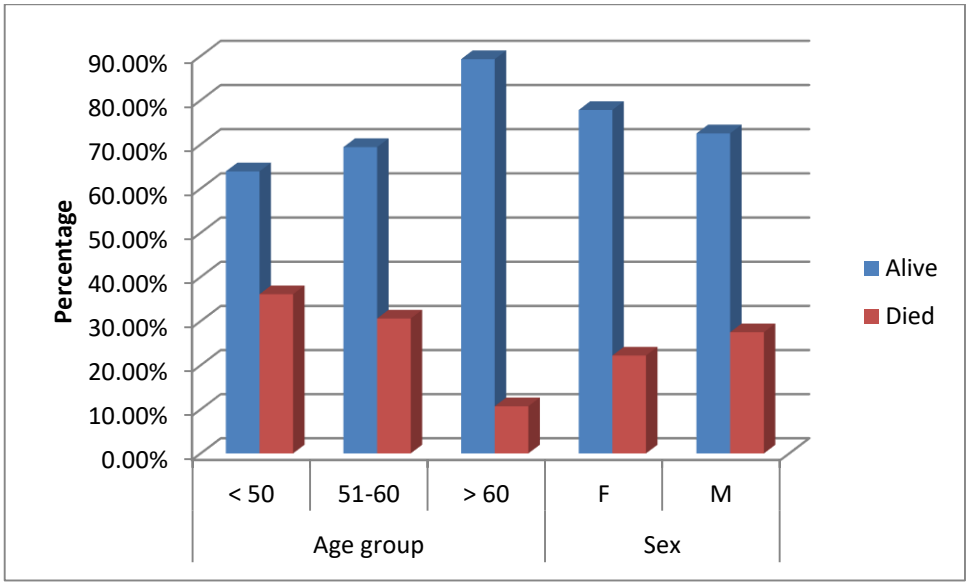
Mean haemoglobin on admission was 9.42 $\pm$ 2.43 mg/dl. Mean TLC at admission was 13.80 + 8.03 (10^3/ul). Mean platelet count at admission was 122.85 + 70.41 (10^3/ul).

UNIVARIATE ANALYSIS OF FACTORS AFFECTING MORTALITY

Table 16 – Relationship of Demographic Factors with Mortality Outcome

		Outcome				Total	Chi-square value	p-value
		Alive		Died				
Age group	< 50	23	63.9%	13	36.1%	36	5.515	0.063
	51-60	25	69.4%	11	30.6%	36		
	> 60	25	89.3%	3	10.7%	28		
Sex	F	7	77.8%	2	22.2%	9	0.115	0.735
	M	66	72.5%	25	27.5%	91		

Figure 13 – Relationship of Demographic Factors with Mortality Outcome

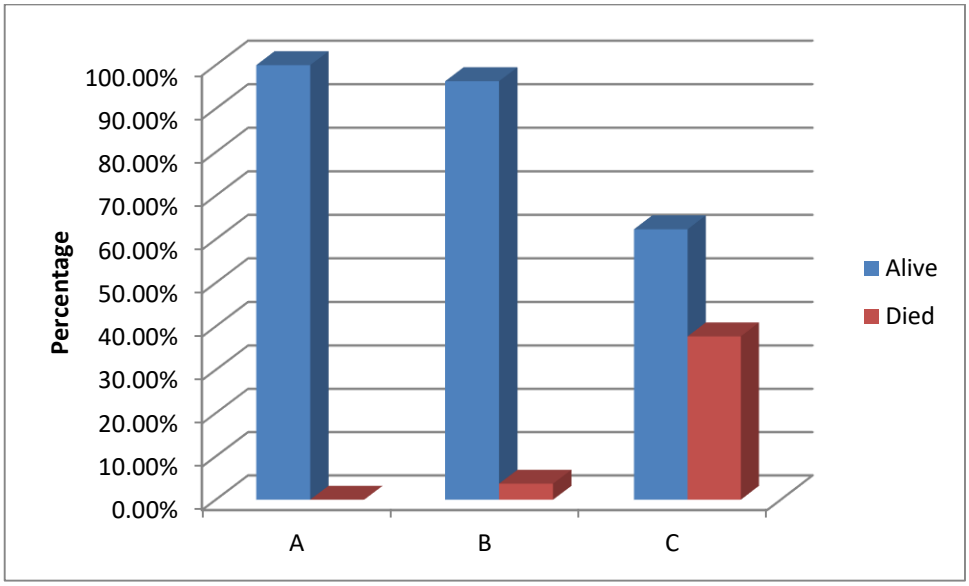


Age and gender of the patient had no significant relationship with the survival or death of the patient as indicated by p value > 0.05.

Table 17- Relationship of CTP Class with Mortality Outcome

		Outcome				Total	Chi-square value	p-value
		Alive		Died				
CTP CLASS	A	4	100.0%	0	0.0%	4	12.908	0.002
	B	26	96.3%	1	3.7%	27		
	C	43	62.3%	26	37.7%	69		
Total		73	73.0%	27	27.0%	100		

Figure 14- Relationship of CTP Class with Mortality Outcome

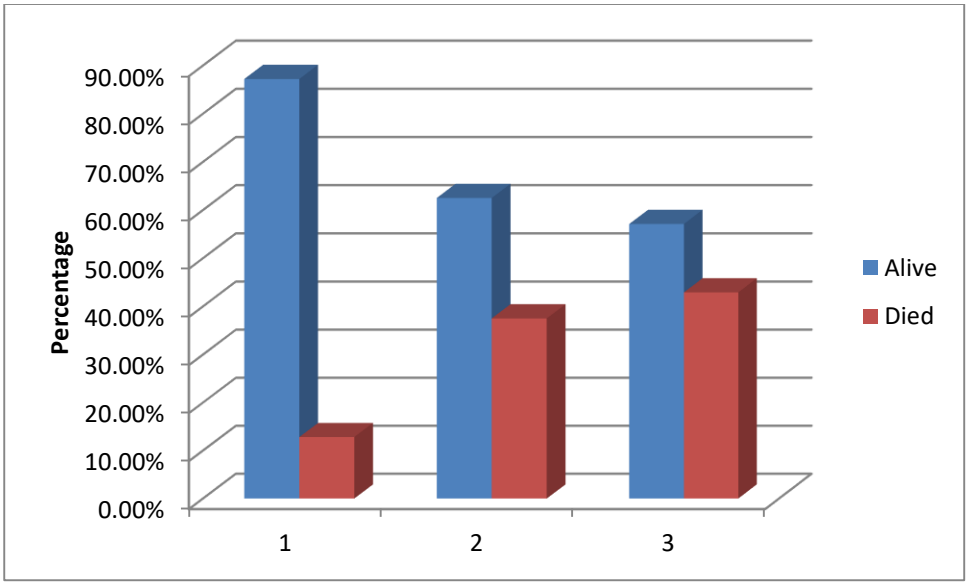


CTP Class of the patient had significant relationship with the mortality outcome as indicated by p value < 0.05. All the patients having CTP Class A survived whereas 3.7% of patients with CTP Class B died and 37.7% patients with CTP Class C died.

Table 18 - Relationship of Stage of AKI with Mortality Outcome

		Outcome				Total	Chi-square value	p-value
		Alive		Died				
AKI Stage	1	41	87.2%	6	12.8%	47	9.300	0.010
	2	20	62.5%	12	37.5%	32		
	3	12	57.1%	9	42.9%	21		

Figure 15 - Relationship of Stage of AKI with Mortality Outcome

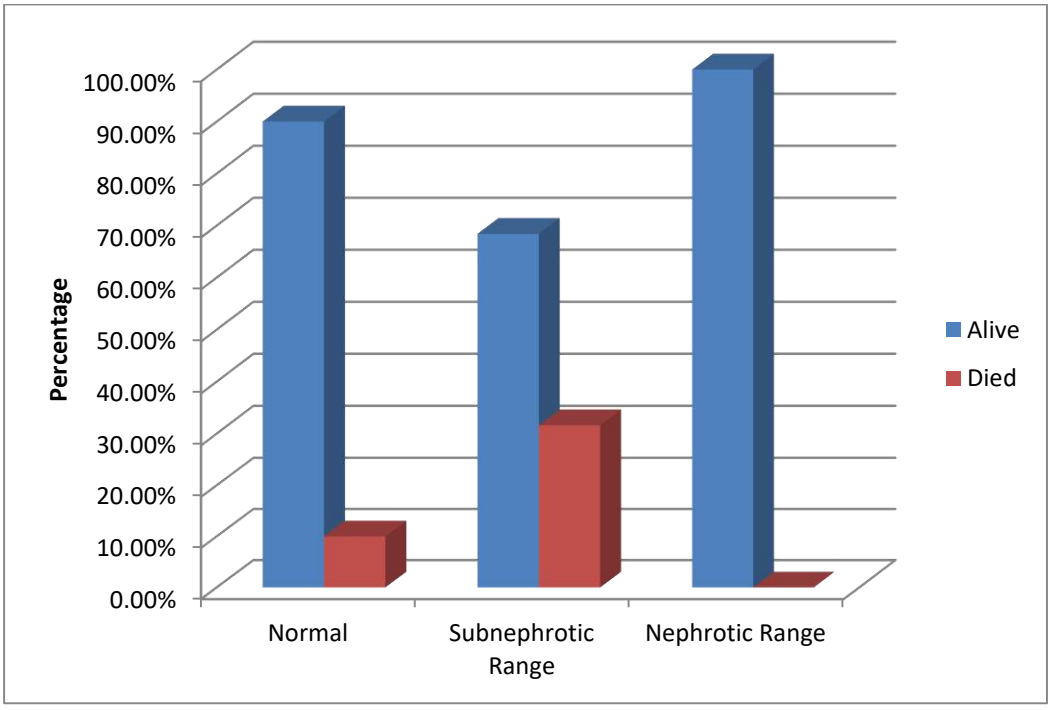


Stage of AKI had a significant relationship with the mortality outcome (p value<0.05). Among the patients with Stage 1 AKI, 87.2% survived whereas 37.5% patients with Stage 2 AKI and and 42.9% patients with Stage 3 AKI died.

Table 19 - Relationship of Range of Proteinuria with Mortality Outcome

		Outcome				Total	Chi-square value	p-value
Proteinuria	**UPCR**	**Alive**		**Dead**				
Normal	<0.15	18	90.0%	2	10.0%	20	4.167	0.124
Subnephrotic Range	0.15-3.5	54	68.4%	25	31.6%	79		
Nephrotic Range	>3.5	1	100.0 %	0	0.0%	1		
Total		73	73.0%	27	27.0%	100		

Figure 16 - Relationship of Range of Proteinuria with Mortality Outcome

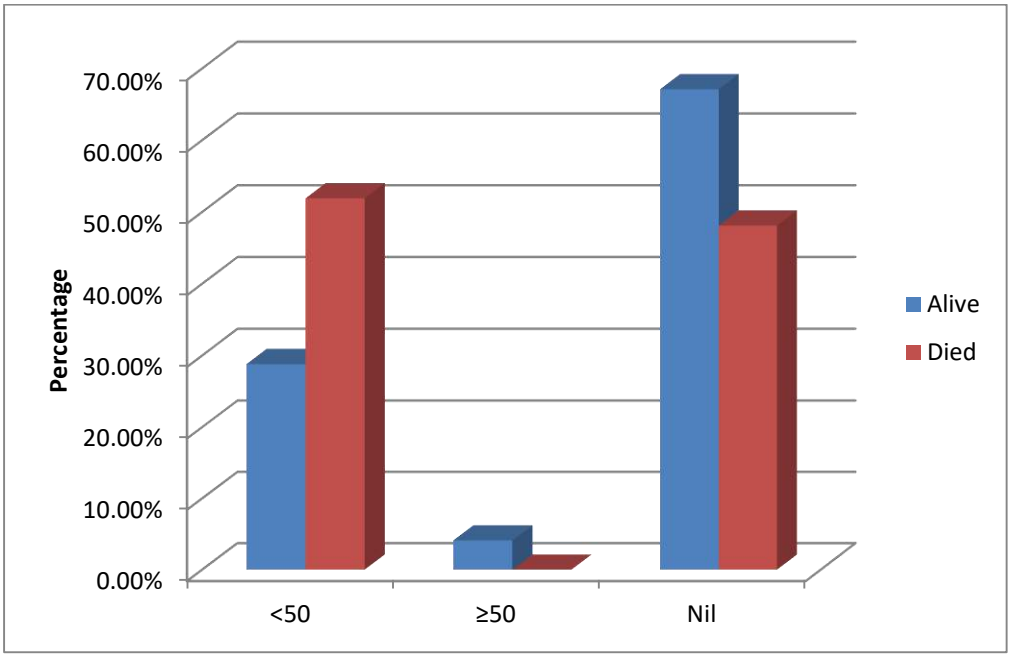


Range of proteinuria had no significant relationship with mortality outcome as shown by p value >0.05.

Table 20 - Relationship of amount of Hematuria with Mortality Outcome

	Outcome				Total	Chi-square value	p-value
RBC/HPF	**Alive**		**Died**				
<50	21	28.80%	14	51.90%	35	5.255	0.072
≥50	3	4.10%	0	0.00%	3		
Nil	49	67.10%	13	48.10%	62		
Total	73	100.00 %	27	100.00 %	100		

Figure 17 - Relationship of amount of Hematuria with Mortality Outcome

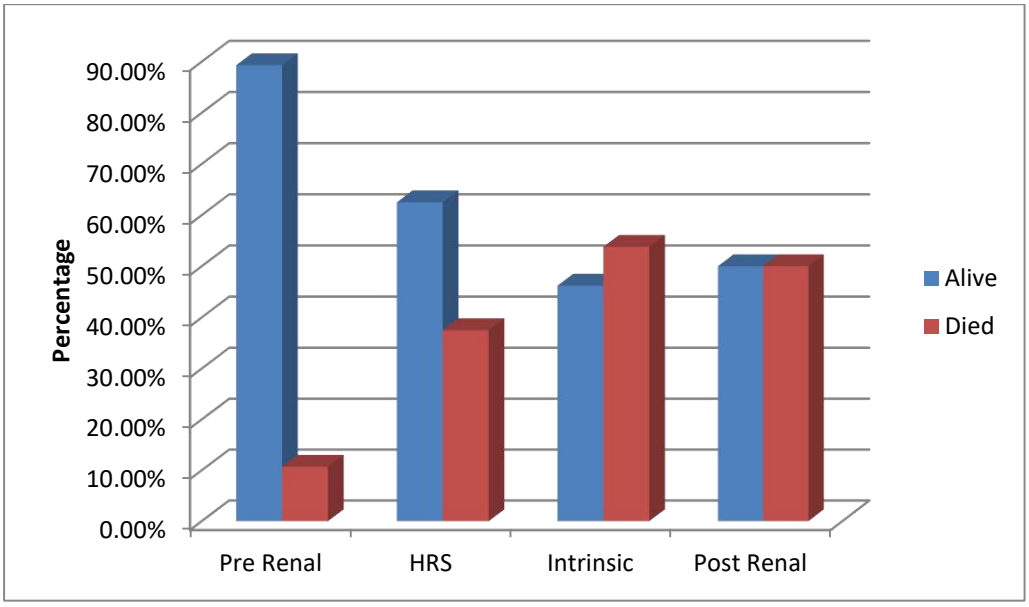


The amount of hematuria had no significant relationship with mortality outcome as shown by p value >0.05.

Table 21 - Relationship of Type of Acute Kidney Injury with Mortality Outcome

		Outcome				Total	Chi-square value	p-value
		Alive		Died				
Type of AKI	Pre Renal	50	89.3%	6	10.7%	56	18.474	0.0001
	HRS	10	62.5%	6	37.5%	16		
	Intrinsic	12	46.2%	14	53.8%	26		
	Post Renal	1	50.0%	1	50.0%	2		

Figure 18 - Relationship of Type of Acute Kidney Injury with Mortality Outcome



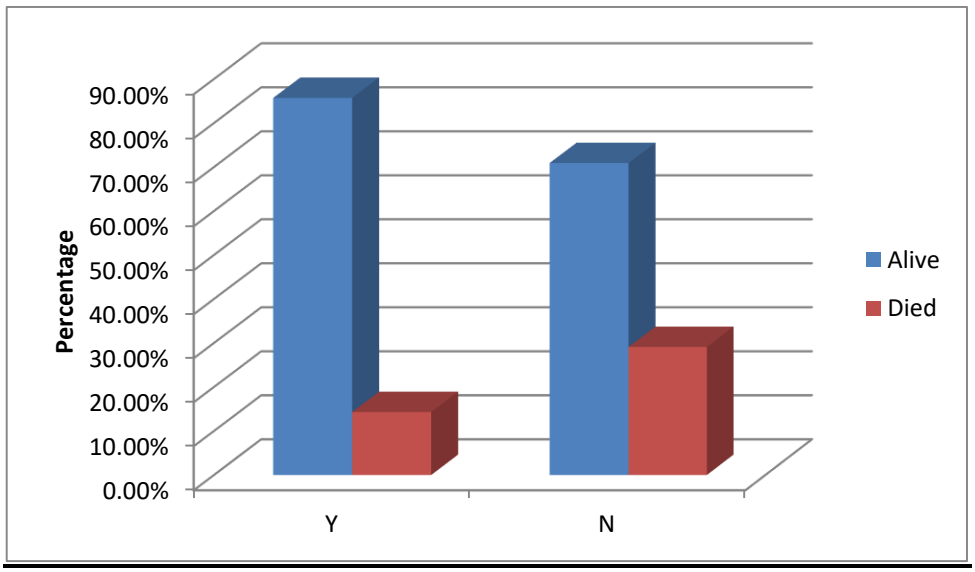
Type of renal dysfunction had significant relationship with the mortality outcome of the patient as indicated by p value < 0.05.

89.3% patients with pre renal AKI survived whereas 37.5% patients with HRS, 50% patients with post renal and 53.8% patients with intrinsic AKI died.

Table 22 - Relationship of Presence of SBP with Mortality Outcome

		Outcome				Total	Chi-square value	p-value
		Alive		Died				
SBP	Y	12	85.7%	2	14.3%	14	1.335	0.248
	N	61	70.9%	25	29.1%	86		

Figure 19 - Relationship of Presence of SBP with Mortality Outcome



Presence of SBP had no significant relationship with the mortality of the patient as indicated by p value > 0.05.

COMPARISION OF MEAN VALUES AMONG MORTALITY GROUPS

Table 23 – Relationship of Mean values of Hepatic Parameters with Mortality Outcome

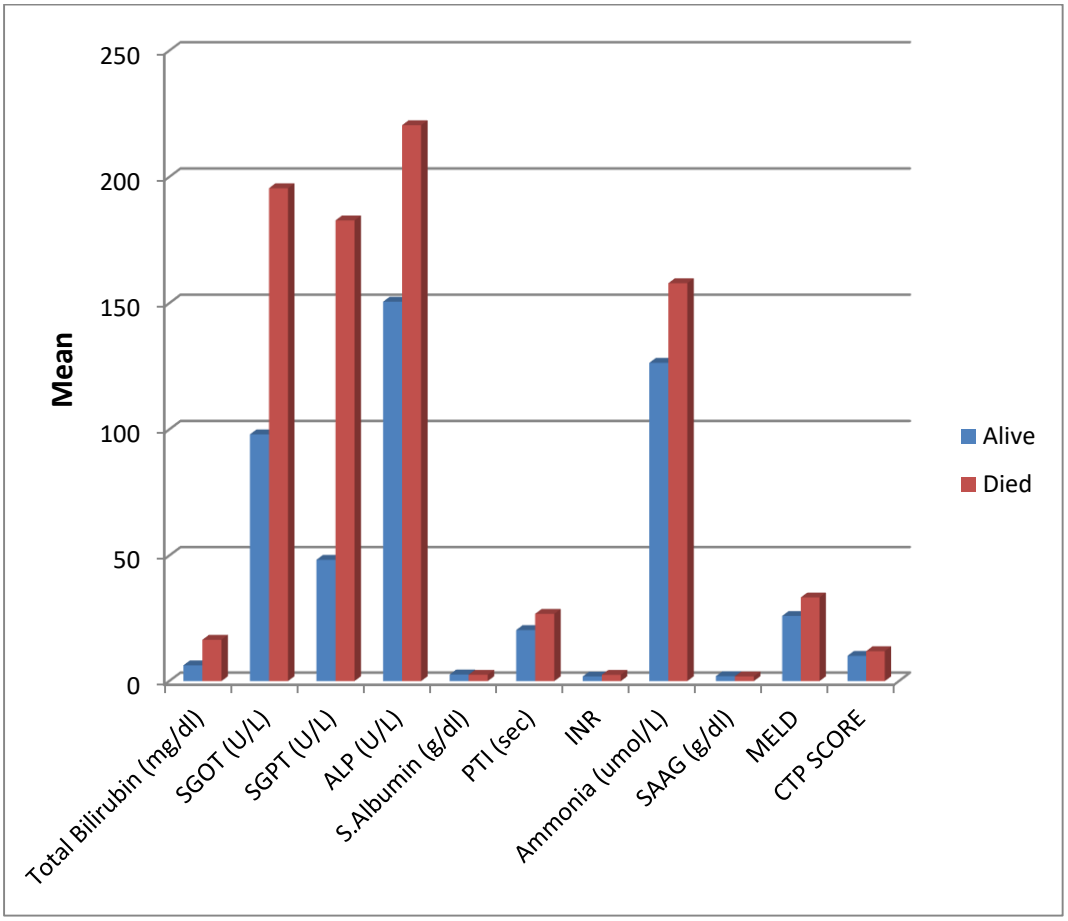
	Alive		Died		t	p-value
	Mean	SD	Mean	SD		
Age	53.85	11.24	49.22	9.28	1.911	0.059

In our study the mean age of the survivors was 53.85 ± 11.24 years and 49.22 ± 9.28 years among those who died. Age had no relationship with mortality outcome as reflected by the p value of >0.05.

Table 24 – Relationship of Mean values of Hepatic Parameters with Mortality Outcome

	Alive		**Died**		**T**	**p-value**
	Mean	**SD**	**Mean**	**SD**		
Total Bilirubin (mg/dl)	6.27	7.42	16.47	12.03	-5.102	0.000
SGOT (U/L)	98.08	96.42	195.56	175.21	-3.536	0.001
SGPT (U/L)	48.33	44.09	182.81	276.94	-4.046	0.000
ALP (U/L)	150.60	95.37	220.52	211.67	-2.278	0.025
S.Albumin (g/dl)	2.64	0.54	2.53	0.58	0.878	0.382
PTI (sec)	20.34	7.41	26.80	11.63	-3.288	0.001
INR	1.86	0.69	2.50	1.14	-3.409	0.001
Ammonia (umol/L)	126.42	75.31	157.96	94.58	-1.518	0.134
SAAG (g/dl)	1.97	0.47	1.89	0.51	0.649	0.518
MELD	25.96	7.49	33.33	6.34	-4.543	0.000
CTP SCORE	10.07	2.19	11.93	1.59	-4.029	0.000

Figure 20 – Relationship of Mean values of Hepatic Parameters with Mortality Outcome

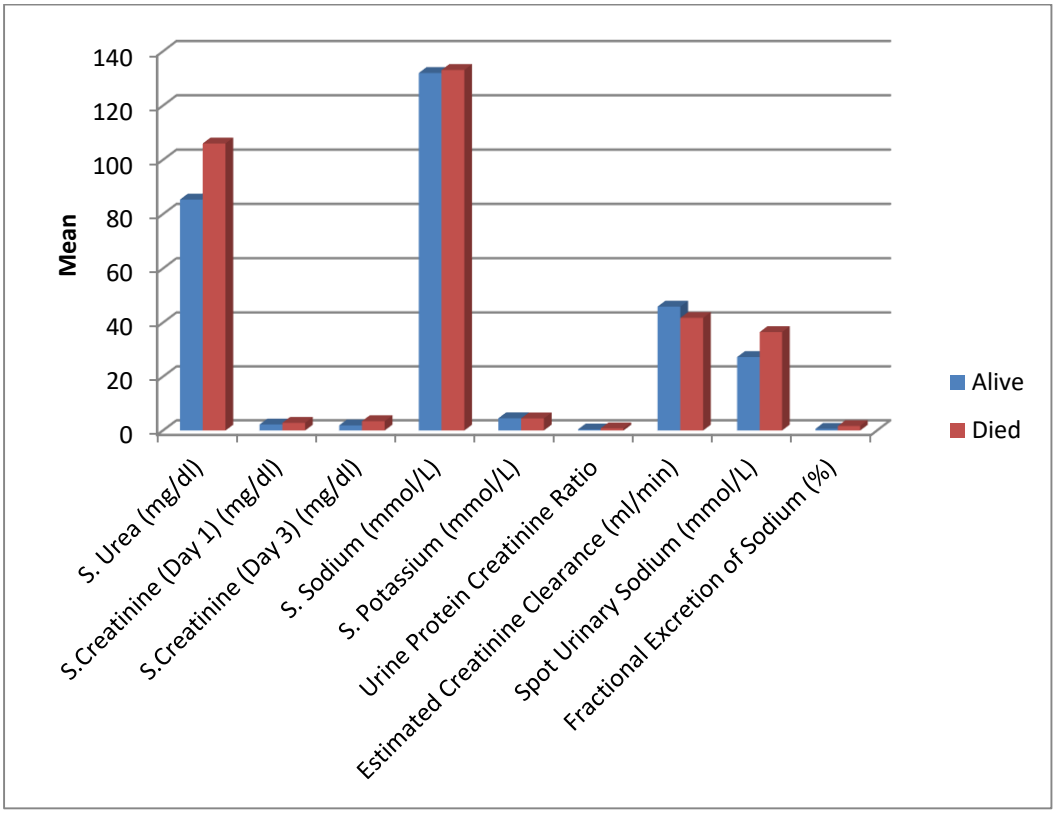


Among the hepatic parameters, mean total bilirubin, SGOT, SGPT, ALP, PTI/INR, MELD Score and CTP Score where higher among non-survivors than survivors and these parameters had significant relationship with the mortality outcome as shown by p value <0.05; whereas S. Albumin, SAAG and Ammonia showed no significant difference as well as no significant relationship with the mortality outcome.

Table 25 – Relationship of Mean values of Renal Parameters with Mortality Outcome

	Alive		Died			
	Mean	**SD**	**Mean**	**SD**	**T**	**p-value**
S. Urea (mg/dl)	85.40	51.98	106.04	62.49	-1.667	0.099
S.Creatinine (Day 1) (mg/dl)	2.24	1.31	2.85	1.72	-1.901	0.060
S.Creatinine (Day 3) (mg/dl)	1.90	1.37	3.47	2.29	-4.201	0.000
S. Sodium (mmol/L)	131.99	6.91	133.11	8.73	-0.672	0.503
S. Potassium (mmol/L)	4.55	0.95	4.50	0.98	0.248	0.805
Urine Protein Creatinine Ratio	0.41	0.61	0.81	0.56	-3.030	0.003
Estimated Creatinine Clearance (ml/min)	45.96	20.56	41.77	25.75	0.844	0.401
Spot Urinary Sodium (mmol/L)	27.27	22.51	36.52	20.46	-1.867	0.065
Fractional Excretion of Sodium (%)	0.64	0.99	1.67	3.25	-2.440	0.016

Figure 21 – Relationship of Mean values of Renal Parameters with Mortality Outcome

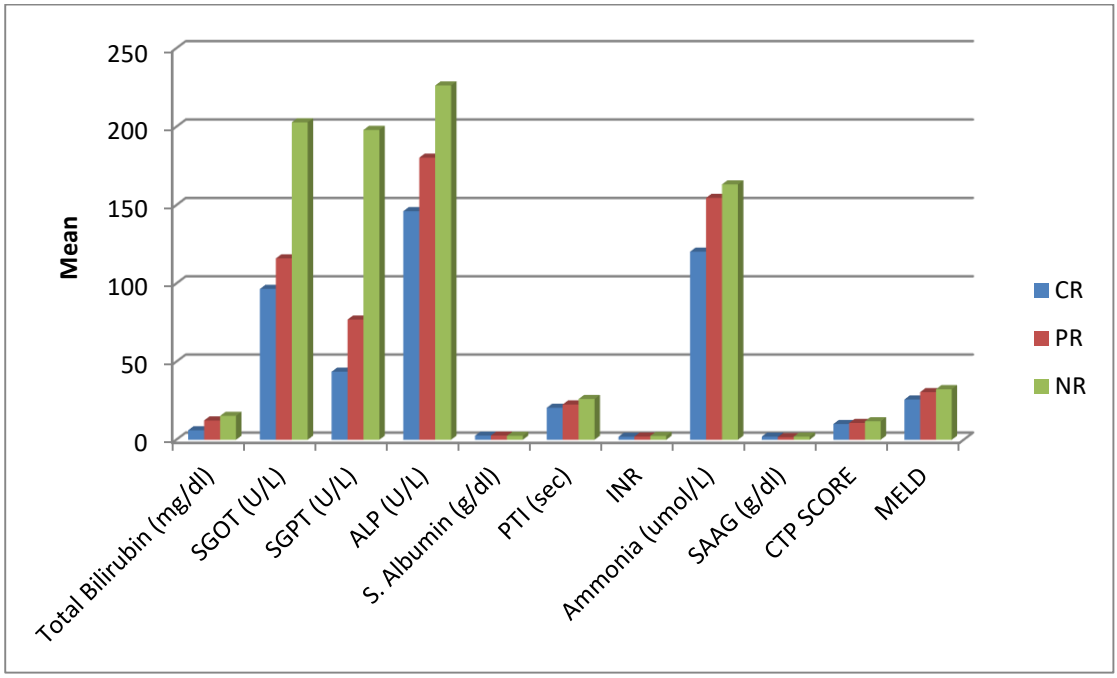


Among the renal parameters, S. Creatinine at day 3 of admission, UPCR and Fractional Excretion of sodium had significant relationship with the mortality outcome, the mean values being significantly higher among non-survivors.

Table 26 – Relationship of Mean values of Hepatic Parameters with Recovery of Acute Kidney Injury

	CR		PR		NR				CR VS PR	CR VS NR	PR VS NR
	Mean	SD	Mean	SD	Mean	SD	F	p-value	p-value	p-value	p-value
Total Bilirubin (mg/dl)	6.06	7.16	12.34	11.59	15.29	12.21	9.748	0.000	0.032	0.000	0.364
SGOT (U/L)	96.58	97.86	116.00	87.41	202.79	182.91	6.587	0.002	0.616	0.000	0.048
SGPT (U/L)	43.58	36.15	77.00	66.29	197.96	290.65	9.748	0.000	0.469	0.000	0.021
ALP (U/L)	146.14	88.67	180.25	117.64	226.33	224.06	3.063	0.051	0.428	0.016	0.341
S. Albumin (g/dl)	2.63	0.56	2.68	0.45	2.51	0.58	0.506	0.604	0.759	0.385	0.389
PTI (sec)	20.48	7.52	22.59	8.28	26.09	12.22	3.460	0.035	0.455	0.010	0.271
INR	1.87	0.70	2.03	0.76	2.44	1.21	3.811	0.026	0.558	0.007	0.182
Ammonia (umol/L)	120.33	76.14	154.60	64.83	163.21	98.73	2.096	0.131	0.236	0.061	0.787
SAAG (g/dl)	1.99	0.48	1.64	0.42	2.00	0.47	2.512	0.088	0.034	0.943	0.050
CTP SCORE	10.06	2.17	10.75	2.05	11.83	1.86	6.321	0.003	0.298	0.001	0.146
MELD	25.81	7.29	30.50	8.82	32.38	6.96	7.661	0.001	0.047	0.000	0.476

Figure 22 – Relationship of Mean values of Hepatic Parameters with Recovery of Acute Kidney Injury

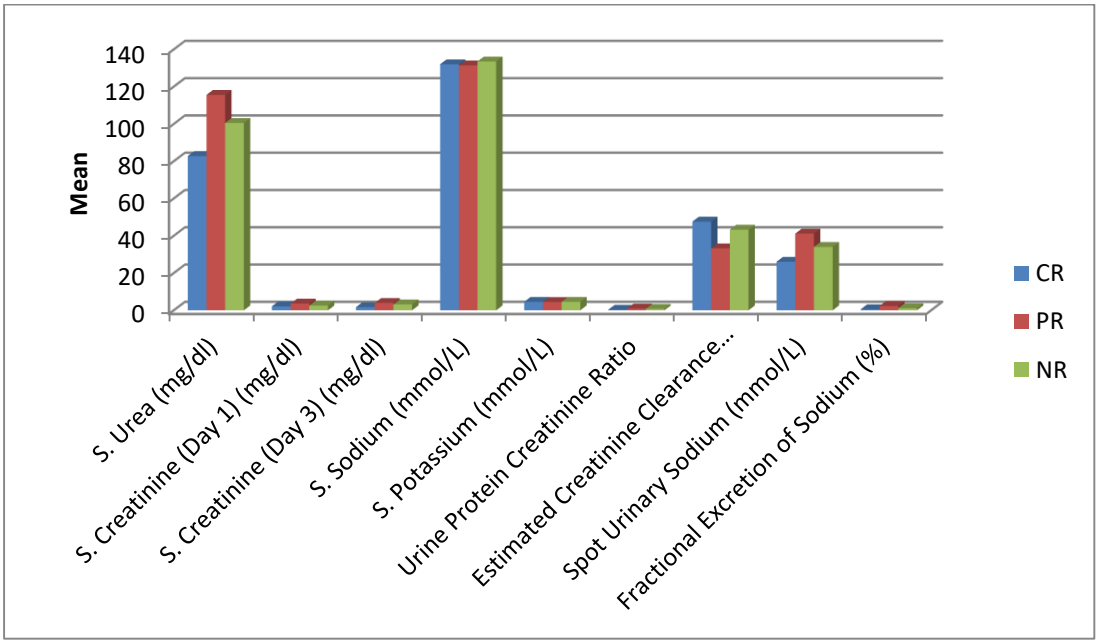


Among the hepatic parameters, Total bilirubin, SGOT, SGPT, PTI/INR, CTP and MELD Score had significant relationship with the recovery of acute kidney injury at the end of hospital stay as evident by p value being <0.05 for these parameters.

Table 27 – Relationship of Mean values of Renal Parameters with Recovery of Acute Kidney Injury

	CR		PR		NR				CR VS PR	CR VS NR	PR VS NR
	Mean	SD	Mean	SD	Mean	SD	F	p-value	p-value	p-value	p-value
S. Urea (mg/dl)	82.78	50.75	115.58	69.48	100.50	57.24	2.292	0.106	0.060	0.179	0.438
S. Creatinine (Day 1) (mg/dl)	2.12	1.08	3.62	2.85	2.56	0.97	6.170	0.003	0.001	0.181	0.033
S. Creatinine (Day 3) (mg/dl)	1.70	1.03	3.96	3.19	3.16	1.71	14.559	0.000	0.000	0.000	0.158
S. Sodium (mmol/L)	132.00	7.20	131.42	5.20	133.50	8.92	0.447	0.641	0.804	0.403	0.431
S. Potassium (mmol/L)	4.56	0.98	4.46	1.06	4.52	0.87	0.056	0.945	0.751	0.865	0.868
Urine Protein Creatinine Ratio	0.33	0.25	0.96	1.39	0.78	0.54	9.536	0.000	0.001	0.001	0.376
Estimated Creatinine Clearance (ml/min)	47.59	20.09	33.23	19.88	43.25	26.46	2.289	0.107	0.038	0.406	0.195
Spot Urinary Sodium (mmol/L)	26.05	20.88	41.17	31.75	34.00	18.22	3.019	0.053	0.030	0.131	0.355
Fractional Excretion of Sodium (%)	0.59	0.98	2.31	4.84	1.10	0.86	4.456	0.014	0.004	0.253	0.070

Figure 23 – Relationship of Mean values of Renal Parameters with Recovery of Acute Kidney Injury

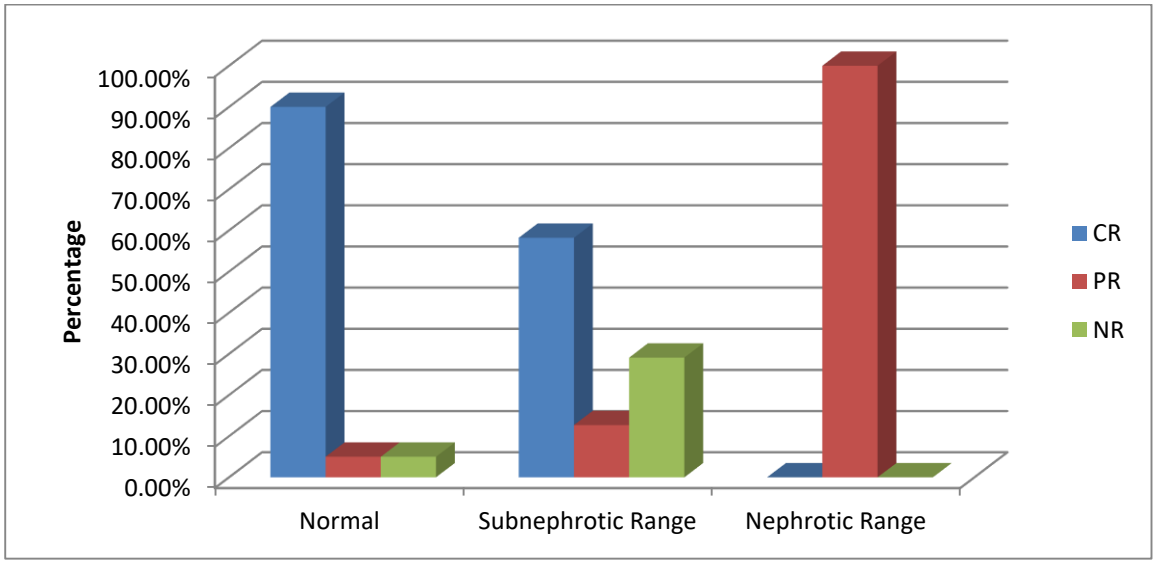


Among the renal parameters, S. Creatinine on day 1 and day 3 of admission, UPCR, and Fractional excretion of sodium had significant relationship with the recovery of acute kidney injury at the end of hospital stay as evident by p value being <0.05 for these parameters.

Table 28 – Relationship of Range of Proteinuria with Recovery of Acute Kidney Injury

		Renal Dysfunction Group						Total	Chi-square value	p-value
Proteinuria	**UPCR**	CR		PR		NR				
Normal	<0.15	18	90.0%	1	5.0%	1	5.0%	20	14.571	0.006
Subnephrotic Range	0.15-3.5	46	58.2%	10	12.7%	23	29.1%	79		
Nephrotic Range	>3.5	0	0.0%	1	100.0%	0	0.0%	1		
Total		64	64.0%	12	12.0%	24	24.0%	100		

Figure 24 – Relationship of Range of Proteinuria with Recovery of Acute Kidney Injury



Amount of proteinuria had significant relationship with the recovery of acute kidney injury at the end of hospital stay as signified by p value <0.05.

Renal functions in 90% of patients with normal range proteinuria recovered completely, 5% recovered partially, and renal function did not recover in 5% of these patients whereas this was seen in only 58.2% patients having subnephrotic range of proteinuria.

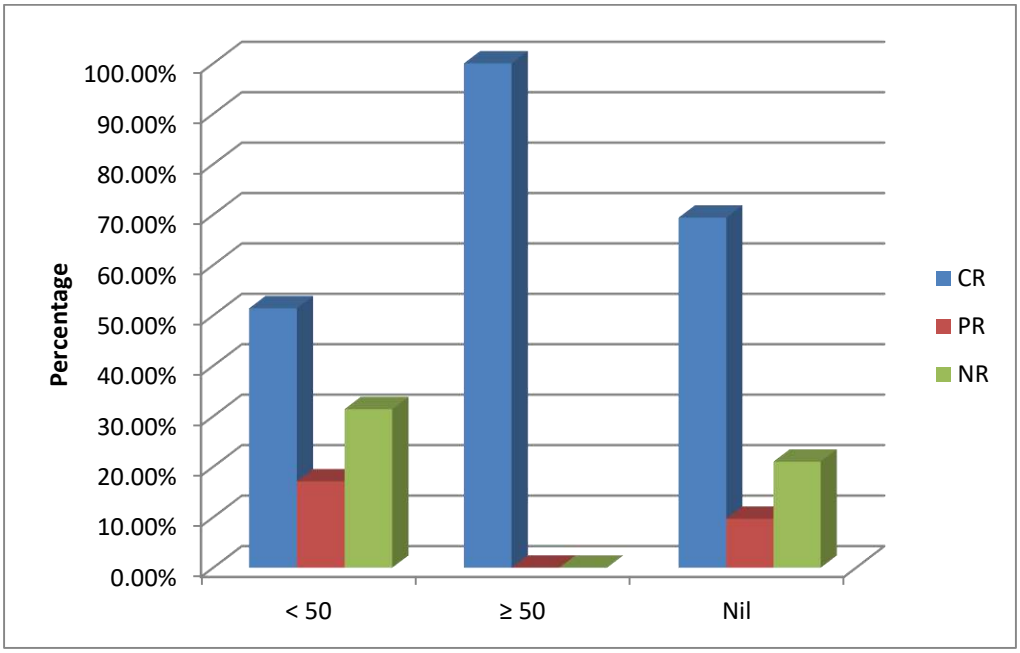
In patients having subnephrotic range proteinuria, renal functions in 58.2% patients recovered completely, in 12.7% patients recovered partially whereas it did not recover in 29.1% patients.

There was only one patient having nephrotic range proteinuria and renal functions recovered partially in that patient.

Table 29 – Relationship of amount of Hematuria with Recovery of Acute Kidney Injury

	Renal Dysfunction Group						Total	Chi-square value	p-value
RBC/HPF	**CR**		**PR**		**NR**				
< 50	18	51.40%	6	17.10%	11	31.40%	35	4.922	0.295
≥ 50	3	100.00%	0	0.00%	0	0.00%	3		
Nil	43	69.40%	6	9.70%	13	21.00%	62		
Total	64	64.00%	12	12.00%	24	24.00%	100		

Figure 25 – Relationship of amount of Hematuria with Recovery of Acute Kidney Injury

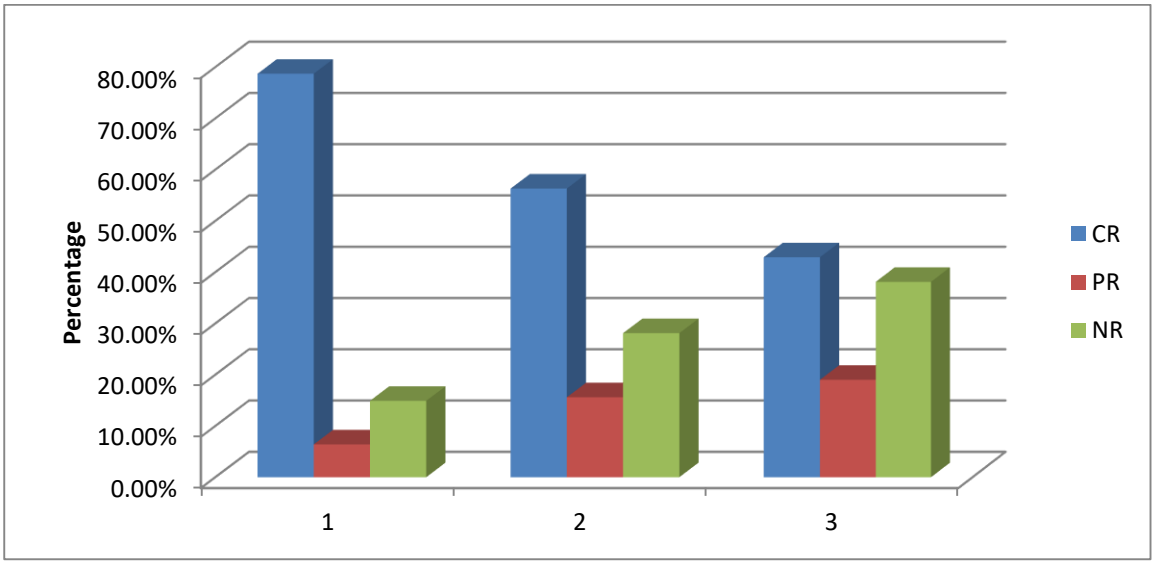


Amount of hematuria had no significant relationship with recovery of acute kidney injury at the end of hospital stay as shown by p value >0.05.

Table 30 – Relationship of Stage of AKI with Recovery of Acute Kidney Injury

		Renal Dysfunction Group						Total	Chi-square value	p-value
		CR		PR		NR				
AKI Stage	1	37	78.7%	3	6.4%	7	14.9%	47	9.404	0.052
	2	18	56.3%	5	15.6%	9	28.1%	32		
	3	9	42.9%	4	19.0%	8	38.1%	21		
Total		64	64.0%	12	12.0%	24	24.0%	100		

Figure 26 – Relationship of Stage of AKI with Recovery of Acute Kidney Injury

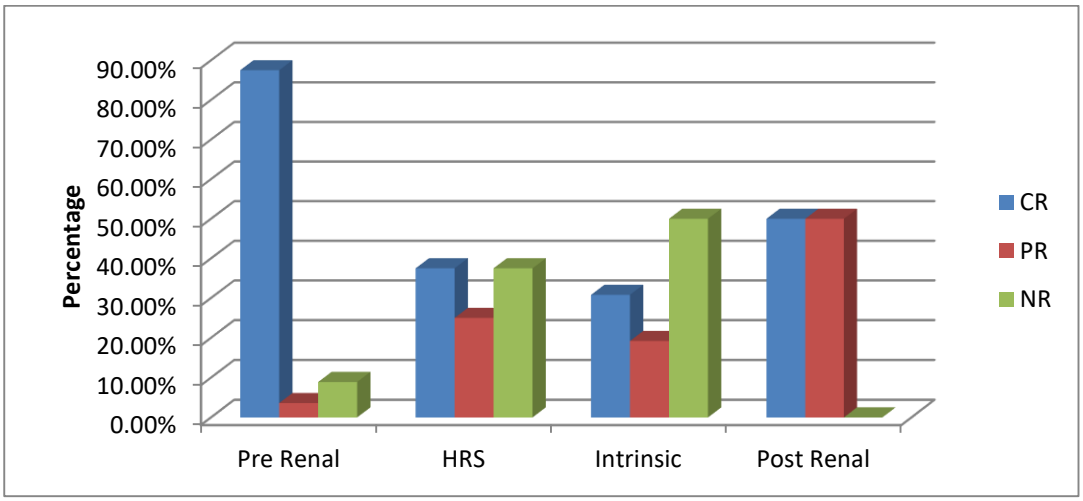


Stage of AKI had no significant relationship with recovery of acute kidney injury at the end of hospital stay as shown by p value >0.05.

Table 31 – Relationship of type of AKI with Recovery of Acute Kidney Injury

		Renal Dysfunction Group						Total	Chi-square value	p-value
		CR		PR		NR				
Type of AKI	Pre Renal	49	87.5%	2	3.6%	5	8.9%	56	34.562	0.0001
	HRS	6	37.5%	4	25.0%	6	37.5%	16		
	Intrinsic	8	30.8%	5	19.2%	13	50.0%	26		
	Post Renal	1	50.0%	1	50.0%	0	0.0%	2		
Total		64	64.0%	12	12.0%	24	24.0%	100		

Figure 27 – Relationship of type of AKI with Recovery of Acute Kidney Injury



The type of AKI had significant relationship with the recovery of acute kidney injury at the end of hospital stay as signified by p value <0.05.

Renal functions in majority (87.5%) of patients with pre renal failure recovered completely.

Patients with HRS had almost equal percentage of patients among the three recovery groups.

Among patients having intrinsic renal failure, renal functions in maximum percentage of patients did not recover (50%).

We had only two patients having post renal type of AKI, of which renal functions in one patient recovered completely whereas renal functions recovered partially in the other at end of hospital stay.

DISCUSSION

This study was an observational study conducted at a tertiary care hospital in North India which included 100 consecutively admitted patients aged ≥ 18 years with liver cirrhosis having AKI. It aimed to study the clinical profile of renal dysfunction in admitted patients with liver cirrhosis and documenting the common causes of acute renal involvement in liver cirrhosis as well as their outcome at the end of hospital stay in terms of mortality and recovery of renal dysfunction.

It was observed that majority of our study population comprised of males (91%), whereas females comprised only 9% of the study population. Mean age of the patients included was 57 years (± 10.89 years) with majority being more than 50 years of age (64%). All patients had established cirrhosis based on clinical presentation, biochemical investigations and radiology data. The most common etiologies of cirrhosis were: Alcohol (50%), non-alcoholic fatty liver disease (20%) and hepatitis B and C (13%). The mean CTP score was10.57 (± 2.20); 4%, 27% and 69% patients had Child A, B and C cirrhosis respectively on admission. The mean MELD score was 27.95 ± 7.89, with 97% patients having a MELD score ≥ 14.

Similar study population characteristics were noted in the studies conducted by Prakash J et al (2010) [77], Soni A et al (2020) [92], Vaz J et al (2020) [93] and Scott RA et al (2013) [38] .

When we analysed the clinical symptomatology in our patients, we found that most of them presented with abdominal distension (73 %), jaundice (51 %), decreased urine output (48%), edema (45%) and altered sensorium (45%). Haemetemesis/Malaena, fever, pain abdomen, vomiting, altered bowel habits were seen in about 26% to 39% of the patients.

Purohit A et al (2019) [94] demonstrated in their study that the most common signs of decompensation of liver in their study were jaundice (78%), followed by ascites (70%), hepatic encephalopathy (37%) and upper GI bleed (30%).

In a similar study by Prakash J et al (2010) [77],of 178 cirrhotic patients with renal diseases, 15 (8.4%) had hematemesis and 29 (16.3%) had malaena at the time of presentation. Pedal edema in 68 (38.2%), ascites in 138 (77.5%) and 62 (34.8%) patients had encephalopathy at admission or developed during course of hospital stay.

These trends can be explained by patients in India seeking help / being diagnosed only once decompensation sets in. Multiple factors can be attributed for this behavior e.g. illiteracy, poverty, lack of universal health insurance and poor health facilities at some places etc. These findings are supported by the results of a large national study from India where 99% of patients with cirrhosis presented with decompensation[95].

Among the hepatic parameters, mean total bilirubin, SGOT, SGPT, ALP, PTI/INR, MELD Score and CTP Score where higher among non-survivors than survivors and these parameters had significant relationship with the mortality outcome (p value <0.05).

Among the renal parameters in our study, S. Creatinine at day 3 of admission, UPCR and FENa had significant relationship with the mortality outcome, the mean values being significantly higher among non-survivors.

In a study by Bohra, A et al (2020) [96] , increased serum bilirubin, urea, creatinine, INR, CTP score, MELD and a MELD score ≥ 15 (*vs* ≤ 15) were significantly associated with a poor prognosis.

The mean Child Pugh score of 10.57 $\pm$ 2.20 and MELD score of 27.95 $\pm$ 7.89 reflects that our population had advanced decompensated liver disease at the time of hospital admission. The relationship of MELD and CTP score with poor prognosis in patients with liver cirrhosis is also corroborated by studies by Botta F et al (2003)[97] and Albers I et al (1989) [98] .

In a study by Prakash J et al (2010) [77], there was significant increase in mortality in patients with class C cirrhosis with renal disease versus class C cirrhosis patients without renal disease, the incidence of renal disease increased with increase in severity of cirrhosis of liver and the

presence of renal disease seemed to have an adverse prognostic impact on class C cirrhosis.

In a study by Keshav R et al [99], statistically significant relationship was found between Child Pugh score and Serum creatinine, suggesting that patients with higher severity of cirrhosis develop renal dysfunction much more commonly.

Similarly, a study by Prakash J et al (2010) [77], added that renal diseases were more frequent with class B and Class C cirrhosis.

In study by Soni A et al (2020) [92] , a positive correlation was seen between CTP Score and renal failure, predicting that more the patient is decompensated higher is the chances to get renal involvement.

The significant relationship of renal failure with mortality outcome was also reflected in a recent large European study of cirrhotic inpatients with and without infections by Moreau R et al (2013) [100], in which acute-on-chronic liver failure (ACLF) defined as two or more organ failures, especially if one organ involved was the kidney, predicted short-term mortality.

The most common type of acute renal dysfunction observed in our study was pre-renal (56%), followed by intrinsic (26%), hepatorenal syndrome (16%) and post renal (2%).

Similar results were seen in studies by Garcia-Tsao G et al. (2008) [11], Fang J-T et al. (2008) [101], and Hartleb M et al. (2012) [25]; in which prerenal causes including hypovolemia and HRS AKI, together accounted for 60% to 70% of all causes of AKI,16 with HRS AKI accounting for 11% to 20% of all causes of AKI.[11,101] Intrinsic renal causes accounted for approximately 30% of all causes of AKI in cirrhotic patients, and included ischemic injury and acute tubular necrosis, acute glomerulonephritis, and acute interstitial nephritis, whereas postrenal (obstructive) causes were seen to be relatively uncommon (<1%).[11,25]

Similarly, in study by Soni A et al (2020) [92] in which pre-renal azotemia formed the majority (47.8% of all renal dysfunction), followed by HRS (28%) and ATN (17.4%).In study by Arora MS et al (2019) [102], prerenal

and HRS were the most usual type of AKI constituting 67.6% and 23.8% of the all AKI respectively.

In a study by Prakash J et al (2010) [77], ATN, HRS and Pre renal failure were seen in 44.4%, 36.4% and 19.2% respectively. In study by Shetty S et al (2018) [103], Acute Tubular Necrosis and Hepato Renal Syndrome were the predominant types of AKI constituting 42.3% and 43.9% of all cases respectively. In their study Prerenalazotemia constituted 13.8% of all cases of AKI. Study from Brazil on cirrhotic patients with AKI, Prerenalazotemia was the main etiology (59.55%) while HRS was in 10.11%.[104]

In studies by Peron JM et al (2005) [105], Moreau R et al (2002) [76], Fang JT et al (2008) [101], in hospitalized patients with cirrhosis, most common cause was prerenal AKI, accounting for approximately 68% of the cases. HRS, which is not volume-responsive, constituted approximately 25% of the cases of prerenal AKI; that is, it accounted for only approximately 17% of cases of AKI in hospitalized patients with cirrhosis.

The type of AKI varies with different studies, this pattern of renal disorder was different from what was observed by Prakash J et al (2010) [77] and Shetty S et al (2018)[103] . However the trend was supported by the data given by Soni A et al (2020)[92], Arora MS et al (2019) [102], and Peron JM et al (2005) [105] , Moreau R et al (2002) [76] , Fang JT et al (2008) [101].

In a study by Scott RA et al (2013) [38] involving patients with liver cirrhosis having AKI: 40% had stage 1 AKI, 29.1% had stage 2 AKI and 30.9% had stage 3 AKI. Mortality increased with each AKI stage; 3.8% in cirrhotics without AKI, 13.5% stage 1, 37.8% stage 2 and 43.2% stage. Worsening liver disease (Child–Pugh class) correlated with increased mortality: 3.1% class A, 23.6% class B and 32.8% class C. Decompensated liver disease (esp. Child–Pugh classes B and C) and AKI were observed to be independent variables predicting death in cirrhotics.

In our study, 47% patients had stage 1 AKI, 32 % had stage 2 AKI & 21% had stage 3 AKI. Presence of AKI showed significant relationship

with the mortality outcome as shown by p value <0.05. Among the patients with Stage 1 AKI, 12.8% died whereas 37.5% patients with Stage 2 AKI and 42.9% patients with Stage 3 AKI died. Worsening liver disease (Child–Pugh class) correlated with increased mortality: 0% in class A, 3.7% in class B and 37.68% in class C (p value <0.05 for trend) which were corroborative with the study by Scott RA et al (2013) [38].

In our study, complete recovery of renal dysfunction occurred in 64 patients prior to discharge. Of the remaining 36 patients, 27 died prior to resolution of renal dysfunction and in the other 12 renal dysfunction improved but did not recover completely (i.e. partially recovered) at the time of discharge.

Our study has few limitations. The spectrum of acute renal dysfunction seen in our study might not be true reflection of the spectrum of acute renal dysfunction in the community because of the small sample size and only hospitalized cirrhotic were included in our study and it was done in a single tertiary care centre and our analysis might be biased by the comparably low variability of several demographic characteristics and patients presenting at a relatively advanced stage of the disease. Also, since the majority of the patients belong to decompensated group i.e. class B and C CTP, this subgroup of patients is expected to have more complications.

This was an observational study done over a short period of time. A prospective study over a longer period of time involving more number of patients will further validate the trends shown in this study. Also follow up of such patients over months to years will determine the long term prognosis of the disease.

Only few studies in India have been done to show the spectrum of renal injury among cirrhotics, hence there is very limited data from our region showing the spectrum of renal injury among patients with cirrhosis. Most of these studies are retrospective and/or they address only a particular subset of renal disorders [e.g., acute renal failure and hepatorenal syndrome (HRS)] rather than the whole spectrum of renal diseases that occurs in cirrhotic patients.

SUMMARY

1. This study included 100 consecutively admitted patients of age ≥ 18 years having chronic liver disease with AKI in the Department of Medicine and allied super specialties of Dayanand Medical College and Hospital, Ludhiana.
2. There were 91% males and 9% females included in the study with mean age of 52.60 ± 10.89 years.
3. Most common etiology of cirrhosis in our study population was alcohol (50%), NASH (20%), Hepatitis B and C related (13%). More than one etiology of cirrhosis was seen in 14% of patients, of which most common was combined HCV and alcohol related, seen in 9% of patients.
4. The most common clinical presentation in patients with liver cirrhosis and AKI were ascites (73%), followed by jaundice (51%), decreased urine output (48%), pedal edema (45%), altered sensorium (45%), hematemesis/malaena (30%).
5. Among the hepatic parameters, mean total bilirubin, SGOT, SGPT, ALP, PTI/INR, MELD Score and CTP Score were predictive of poor prognosis.
6. Majority of the patients had CTP Class C (69%) followed by CTP Class B (27%). Mean MELD Score was 27.95 ± 7.89.
7. Proteinuria was seen in 80% cases (nephrotic range in 1% and sub-nephrotic range in 79%), microscopic hematuria was seen in 38% cases (significant in 35% cases and insignificant in 3% cases)
8. Among the renal parameters, higher S. Creatinine at day 3 of admission, UPCR and Fractional Excretion of sodium were predictive of poor prognosis.
9. The most common type of acute renal dysfunction observed was Pre- renal (56%), followed by Intrinsic (26%), HRS (16%), post renal (2%).
10. Higher the stage of AKI, lesser the chances of recovery of AKI and more the mortality.

11. At the end of hospital stay, renal functions recovered completely in majority of patients (64%), recovered partially in 12 % of the patients, and did not recover in 24% of the patients.
12. In terms of mortality outcome at the end of hospital stay, 73% patients survived and were discharged whereas 27 % of the patients of liver cirrhosis admitted with acute renal dysfunction expired.
13. Maximum mortality was seen with intrinsic type of AKI (53.8%), followed by post renal AKI (50%) and HRS (37.5%). Minimum mortality was seen with pre-renal AKI (10.7%).
14. The factors predicting mortality were presence of severe jaundice, transaminitis, coagulopathy, higher Child Pugh score and MELD Score among hepatic parameters, and severity of renal failure, UPCR, FENa among renal parameters.

CONCLUSION

Acute kidney injury (AKI) is a common complication of liver cirrhosis and is of the utmost clinical and prognostic relevance.

The etiology of renal diseases in the cirrhotic patients is varied. Correct differentiation is imperative, as treatment differs substantially. While pre-renal AKI usually responds well to plasma volume expansion, HRS-AKI and ATN require different specific approaches and are associated with substantial mortality.

Hence, our study is important because we analysed data of the complete spectrum of renal disorders among hospitalized patients with cirrhosis which helps in early recognition of the type of acute kidney injury so that timely healthcare interventions can be done to prevent the substantial morbidity and mortality. Higher CTP and MELD Score and higher AKI Stage were seen to be predictive of poor mortality outcome in this study.

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				Presenting Complaints										Past History					Drug History											GPE			Systemic Examination														
														Cirrhosis																																	
S.No.	MRD No.	Name	Age/Sex	Jaundice	Edema	AD	H/M	AS	Fever	PA	Vomiting	ABH	DUO	Duration	Etiology	J	VB	CoNmorbidities	Diuretics	Laxatives	NSAIDs	Comp & Alt Med	Nephrotoxic Antibiotics	Beta Blockers	Antiplatelet + Statin	Contrast	OHA	Shock	J	E	Flaps	P/A (FF)	Urea	S.Cr (Day 1)	S.Cr. (Day 3)	Total Bilirubin	SGOT	SGPT	ALP	Na	K	S.Alb	PTI/INR	Ammonia	UPCR
1	664602	PM	54/M	N	N	Y	N	N	N	N	N	N	Y	1.5 years	ALD	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	118	6.2	4.8	1.6	34	14	147	131	6.2	2.5	18.9/1.72	115	0.2
2	702095	AS	43/M	Y	Y	Y	N	Y	N	Y	N	N	Y	1 year	ALD	Y	Y	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	65	1.36	1.19	5.95	46	25	84	131	3	1.8	30.5/2.77	165	0.1
3	635843	NS	50/M	Y	Y	Y	N	Y	N	N	N	Y	Y	2 weeks	HCV & ALD	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	69	2.21	1.8	29.05	119	63	147	128	2.4	2.5	31.2/2.83	65	0.4
4	724604	BS	46/M	Y	Y	Y	N	N	N	N	Y	N	N	10 days	ALD	N	N	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	106	2.95	2.3	22.93	72	29	78	128	5	2.3	25.3/2.30	27	0.4
5	99602	NS	62/M	N	N	N	N	Y	N	N	N	N	N	7 years	ALD	Y	Y	DM II	N	Y	N	N	N	N	N	N	N	N	N	N	N	Y	N	71	2.21	1.6	1.63	52	22	185	139	4.6	3.84	13.9/1.27	155	0.13
6	739039	RK	62/M	N	N	Y	N	Y	N	N	N	N	N	3 years	ALD	Y	N	DM II	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	95	1.83	1.2	1.09	24	13	156	123	5.4	3.22	12.7/1.16	78	0.5
7	749245	DL	51/M	Y	N	Y	N	N	N	N	N	N	N	1.5 years	HBV	N	N	N	Y	N	N	N	N	N	N	N	N	Y	Y	N	N	Y	63	1.45	1	13.82	67	21	90	133	5.5	2.88	34.2 /3.14	N.D	0.3
8	759005	AK	48/M	Y	N	N	N	N	N	Y	Y	Y	Y	6 years	HBV + ALD	Y	Y	N	Y	N	N	N	N	N	N	N	N	Y	Y	N	N	N	65	2.56	1.6	6.89	61	38	104	129	4.2	2.12	55.8/5.12	108	0.2
9	623666	TR	63/M	N	N	Y	N	Y	N	Y	N	N	Y	5 years	ALD	N	Y	DM II	N	N	N	N	N	N	N	N	N	Y	N	Y	Y	Y	106	4.11	2.9	5.6	88	47	249	126	7.5	2.16	17.3/1.59	175	0.6
10	776699	NS	35/M	Y	Y	Y	N	N	Y	N	N	N	N	RD	HCV	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	N	Y	72	1.35	0.6	22.7	86	56	126	130	4	3.3	19.3/1.77	N.D	0.1
11	236838	RC	68/M	Y	N	N	N	N	Y	Y	N	N	N	3 years	ALD	Y	N	DM II	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	153	2.87	3.5	9.07	36	25	167	124	4.6	3.15	16.9/1.55	N.D	0.8
12	800391	NS	38/M	Y	N	N	Y	Y	N	N	N	N	N	RD	ALD	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	Y	N	39	1.74	1.2	7.73	270	38	150	139	5.3	1.97	24.3/2.23	213	0.1
13	796914	BS	50/M	N	N	Y	N	N	N	N	Y	N	N	7 months	HBV	N	Y	DM II	N	N	N	N	N	N	N	N	N	N	Y	N	N	Y	47	1.25	2.1	1.24	78	54	102	137	5	2.63	17.6/1.61	N.D	0.2
14	772784	SK	47/M	Y	N	Y	N	Y	N	N	N	N	N	1 year	ALD	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	Y	Y	38	2.55	1.6	19.27	152	30	69	129	2.9	3.4	18.5/1.70	107	0.1
15	901546	PS	52/M	N	N	Y	N	Y	Y	N	N	Y	Y	3 years	HBV + ALD	Y	N	N	N	N	Y	Y	N	N	N	N	N	N	Y	N	Y	Y	163	7.98	6.5	2.75	85	47	193	130	5.8	2.18	14.9/1.37	131	0.17
16	444518	UK	61/F	Y	Y	Y	N	Y	N	N	N	Y	Y	3 years	NASH	N	N	DM II, Hypothyroid	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	129	2.07	1.98	6.13	57	42	269	106	5.9	3.15	20.5/1.88	67	0.8
17	457248	MG	57/M	N	Y	Y	N	Y	N	N	N	Y	Y	2 years	NASH	N	N	DM II, CAD, Obesity	N	N	N	N	N	N	N	N	N	Y	N	Y	Y	Y	31	1.39	1.25	5.22	80	34	43	118	4.2	2.63	33.4/3.06	488	1.106
18	34255	SS	53/M	N	Y	Y	N	N	N	N	N	N	N	9 years	ALD	Y	N	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	74	1.38	1.26	3.83	54	32	149	135	4.4	1.82	18.7/1.72	75	0.9
19	909397	TG	52/M	Y	N	Y	Y	Y	Y	Y	Y	N	N	20 days	ALD	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	148	3.08	4.5	35.84	217	108	193	124	2.7	2.59	61.4/5.63	233	1
20	904288	KS	40/M	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	2 years	ALD	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	271	10.21	11.4	23.17	91	67	221	134	3.9	2.19	32.3/2.96	194	1.9
21	761719	MS	38/M	Y	N	Y	Y	N	N	N	N	N	N	4 years	ALD	Y	Y	Chr. Pancreatitis	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	43	1.26	1.35	4.28	115	58	112	138	4.5	2.53	16.1/1.53	173	0.5
22	885606	SK	47/M	Y	Y	Y	N	Y	N	N	N	N	Y	5 years	NASH	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	84	2.85	2.16	5.7	30	16	59	128	5.3	1.97	25.0/2.29	132	0.81
23	910260	JS	55/M	N	N	Y	Y	Y	N	N	Y	N	Y	1.5 months	HCV	N	N	HTN	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	80	2.1	1.5	1.67	72	48	100	133	4.2	2.98	14.9/1.37	99	0.4
24	903787	KR	62/M	N	N	N	Y	Y	N	N	N	N	N	RD	NASH	N	N	DM II	N	N	N	N	N	N	N	N	N	Y	N	N	Y	Y	131	2.17	3.2	2.24	109	63	182	138	4.8	1.52	30.0/2.75	164	0.8
25	975399	LS	47/M	Y	N	Y	Y	N	N	Y	N	Y	N	4 months	ALD	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	Y	45	1.78	1.34	24.37	63	30	100	132	4.1	2.76	36.3/3.29	101	0.21
26	976336	NS	58/M	Y	N	Y	N	Y	N	N	N	Y	N	3 days	ALD + NASH	N	N	N	Y	N	N	N	N	N	N	N	N	N	Y	N	Y	N	54	2.4	4.5	25.92	232	70	151	124	6.3	3.61	33.3/3.02	66	0.1
27	971562	JS	50/M	Y	Y	Y	Y	Y	Y	N	N	N	Y	1 year	ALD	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	Y	152	1.83	2.1	11.94	126	163	120	129	5.3	3.46	25.7/2.34	47	0.3
28	963735	NK	55/M	N	N	N	Y	Y	N	N	Y	N	N	1 month	NASH	N	Y	Obesity	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	85	1.46	1.18	0.61	64	46	108	136	4.9	3.57	19.9/1.81	39	0.6
29	979729	BSB	53/M	Y	N	Y	Y	Y	N	Y	N	Y	Y	4 years	HCV + ALD	N	N	CAD	N	N	N	N	N	N	N	N	N	N	Y	N	Y	Y	224	4.02	4.2	23.42	246	79	81	135	3.8	2.16	41.4/3.75	106	0.2
30	640959	AK	35/M	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	2 years	ALD	Y	N	N	N	N	Y	N	N	N	N	N	N	N	Y	Y	Y	Y	93	3.65	3.8	1.16	107	25	110	143	5.7	2.46	16.9/1.54	216	0.1
31	976443	JPS	62/M	Y	N	N	N	Y	Y	N	N	Y	Y	1 month	ALD	N	N	N	Y	N	N	N	N	N	N	N	N	Y	Y	N	Y	N	89	2.06	2.9	34.17	48	51	214	130	3.8	2.73	14.2/1.30	70	1.6
32	979671	JS	58/M	N	N	Y	N	Y	N	N	N	Y	N	2 days	HBV + ALD	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	Y	Y	65	2.26	1.35	2.94	44	18	82	127	4.2	1.74	20.1/1.83	97	0.4
33	972222	GS	36/M	Y	N	Y	N	N	Y	N	N	N	Y	2 years	ALD	Y	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	Y	Y	107	3.16	2.9	31.41	75	27	183	120	2.6	2.76	35.7/3.24	N.D	0.9
34	923948	KS	50/M	Y	N	Y	N	N	N	Y	Y	Y	Y	7 months	ALD	Y	Y	N	Y	N	N	N	N	N	N	N	N	N	Y	N	N	Y	108	2.26	1.98	7.3	212	71	167	132	4.4	2.69	20.1/1.83	161	0.2
35	965402	MS	42/M	Y	N	Y	N	N	Y	N	Y	N	Y	3 months	HCV + ALD	Y	Y	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N	Y	198	3.6	4.5	10.5	320	396	210	128	4.5	3	19.6/1.9	N.D	0.8
36	980716	GS	30/M	Y	Y	Y	Y	N	N	N	Y	Y	N	6 months	ALD	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	N	Y	18	1.23	1.8	6.11	90	36	50	139	5.4	1.79	22.7/2.07	158	0.34
37	980418	SS	64/M	N	N	N	Y	N	N	N	Y	N	N	RD	ALD	N	N	CAD	N	N	N	N	N	Y	N	N	N	Y	N	N	N	N	145	1.67	1.36	0.65	411	126	107	132	5.2	2.52	18.0/1.64	60	0.2
38	982231	AM	53/M	Y	N	Y	N	Y	Y	N	N	N	Y	9 months	ALD	N	N	DM II, HTN	Y	Y	N	N	N	N	N	N	N	Y	Y	N	Y	Y	148	2.57	5.88	9.28	172	24	340	145	4.4	3.55	18.1/1.65	375	1.8
39	980523	ZSJ	43/M	Y	N	Y	N	N	N	N	N	N	Y	1 month	ALD	N	N	HTN	N	N	N	N	N	N	N	N	N	N	Y	N	N	Y	42	2.02	1.68	23.79	97	50	123	129	4.5	2.65	40.7/3.69	66	0.4
40	84322	DL	64/M	N	N	N	N	Y	N	N	N	N	Y	7 years	ALD + NASH	N	Y	DM II, CAD	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	41	1.22	1.18	2.41	70	29	114	130	3.8	2.58	18.0/1.64	86	0.1
41	980279	SS	58/M	N	Y	N	N	Y	N	N	N	Y	N	2 years	HCV	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N	67	1.78	1.03	1.8	35	33	51	139	4.7	2.84	17.5/1.60	141	0.16
42	981092	V	42/M	Y	Y	Y	Y	Y	N	Y	Y	N	N	1 month	ALD	N	N	HTN	N	N	N	N	N	N	N	N	N	N	Y	Y	N	Y	69	1.49	1.35	25.17	159	101	128	137	3.8	2.39	27.8/2.53	175	0.75
43	31095	SK	51/M	Y	Y	N	N	Y	Y	Y	N	Y	N	4 years	ALD	N	N	HTN, CAD	Y	N	N	N	Y	N	N	N	N	N	Y	Y	Y	N	103	2.34	1.4	11.88	74	26	70	130	4.9	2.14	28.2/2.56	77	0.14
44	979674	SS	52/M	N	N	N	Y	Y	Y	N	Y	Y	N	13 years	ALD	Y	N	DM II, HTN	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	54	1.23	0.66	2.41	26	26	124	128	7	2.6	17.3/1.58	123	0.3
45	977726	SS	49/M	N	Y	Y	Y	N	N	N	N	Y	N	RD	ALD	N	Y	N	Y	N	N	N	N	N	N	N	N	Y	N	N	N	Y	72	2.33	2.4	2.43	87	29	149	131	3.3	1.94	26.0/2.36	56	0.3
46	981651	SS	45/M	N	Y	Y	Y	N	Y	Y	Y	Y	Y	3 years	ALD	Y	N	N	Y	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	267	5.74	3.38	2.96	90	33	116	126	3.8	1.59	27.0/2.45	N.D	0.5
47	531835	JJ	71/M	N	N	N	Y	Y	N	N	Y	N	N	2 years	NASH	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	Y	82	1.78	1.92	0.94	82	55	484	138	3.6	2.41	11.8/1.08	170	0.97
48	983526	MS	70/M	N	Y	N	N	N	Y	N	N	N	Y	3 years	HCV	N	Y	DM II	N	N	N	N	N	N	N	N	N	Y	N	Y	N	N	60	1.28	0.99	1.1	30	18	41	134	4.2	3.9	23.0/2.09	N.D	0.2
49	983511	PK	45/M	N	Y	Y	N	N	N	N	N	N	N	RD	NASH	N	N	N	N	N	Y	N	N	N	N	N	N	N	Y	N	Y	Y	73	1.36	0.94	0.88	79	48	356	135	4.8	2.52	13.8/1.26	N.D	0.4
50	981142	JS	47/M	N	Y	Y	N	N	N	N	N	N	N	RD	ALD	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	Y	Y	51	1.57	0.89	2.04	29	11	41	144	2.6	1.36	21.8/1.99	130	0.11
51	934040	OP	65/M	N	N	Y	N	N	N	N	N	N	Y	5 months	ALD + HBV	N	N	Ac. on chr pancreatiti, CAD, Hypothyroid	N	N	N	N	N	N	N	N	N	Y	N	Y	Y	Y	56	1.56	1.32	1.36	55	20	138	114	3.2	2.11	14.4/1.32	66	0.2
52	984336	BK	55/F	N	N	Y	Y	Y	N	N	Y	N	N	5 years	HCV	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	Y	55	1.28	0.5	2.45	83	55	108	137	4.6	3.4	21.5/1.96	176	0.4
53	984199	SS	60/M	N	N	Y	Y	N	N	N	N	Y	N	5 years	NASH	N	N	Obesity	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	54	1.26	1.3	1.38	27	23	84	136	4.2	3.11	16.7/1.53	N.D	0.31
54	648172	VD	56/F	N	Y	Y	N	N	N	N	N	Y	Y	1 month	NASH	N	Y	DM II, HTN, Hypothyroid	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	51	1.75	1.39	0.63	26	10	174	135	4.7	2.68	18.1/1.6	N.D	5.1
55	984060	BS	54/M	Y	Y	Y	N	N	N	N	N	N	N	1 year	ALD	Y	N	N	Y	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	76	2.12	1.69	12.48	42	16	107	132	4.9	2	25.0/2.27	N.D	0.1
56	861457	PKP	65/M	N	Y	Y	Y	N	N	N	N	N	N	1 year	ALD	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	Y	N	Y	99	3.04	1.32	3.29	129	23	122	123	5.7	2.87	15.8/1.44	65	0.2
57	757398	JS	33/M	N	Y	N	N	N	N	N	N	N	Y	1 years	ALD	N	N	N	Y	N	N	N	N	N	N	N	N	Y	Y	Y	N	Y	35	3.65	4.52	4.64	55	11	81	128	5.3	2.74	25.0/2.27	N.D	2.1
58	873542	LR	52/F	Y	Y	Y	N	N	N	N	N	N	N	4 months	NASH	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	131	2.72	2.05	5.55	58	35	137	126	4.9	2.14	23.0/2.11	74	0.5
59	68025	RS	63/M	N	N	Y	N	Y	N	N	N	N	N	4 years	NASH	Y	N	DM II, Psoriasis	N	N	N	N	N	N	N	N	N	N	Y	N	N	Y	36	1.28	0.85	3.14	87	42	122	134	4.4	2.54	16.9/1.55	96	0.8
60	873667	MK	45/M	N	N	Y	N	N	N	N	N	N	N	6 months	NASH	N	Y	DM II	N	N	N	N	N	N	N	N	N	N	Y	N	N	Y	38	1.26	0.86	2.43	85	21	323	140	3	3.12	15.4/1.41	N.D	0.2
61	509550	N	61/M	N	Y	N	N	Y	N	N	N	N	Y	1 year	NASH	N	N	DM II, HTN	N	N	N	N	N	N	N	N	N	N	N	Y	Y	N	102	1.42	1.35	1.05	68	55	217	128	5.7	2.69	13.6/1.25	167	0.7
62	875369	DS	60/M	Y	Y	Y	N	N	Y	N	N	N	N	3 years	ALD	N	Y	DM II	Y	N	Y	N	N	Y	N	N	N	N	Y	Y	Y	Y	66	1.54	1.5	10.21	49	14	112	127	4.9	2.27	19.0/1.74	N.D	0.3
63	913187	SS	47/M	Y	Y	Y	N	N	N	N	N	N	N	2 months	ALD + NASH	Y	N	DM II, HTN, Hypothyroid, Obesity	N	N	N	Y	N	N	N	N	N	N	Y	Y	N	Y	31	1.54	1	1.75	36	21	68	138	4.1	2.44	15.9/1.46	N.D	0.09
64	978943	BR	55/M	N	Y	Y	Y	N	N	N	N	Y	N	10 years	ALD	Y	Y	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	60	1.47	1.12	2.54	59	29	84	131	5.3	2.41	23.1/2.10	87	0.3
65	988775	DS	48/M	Y	Y	Y	N	N	N	Y	Y	N	N	15 days	ALD	Y	N	DM II, HTN	Y	N	N	N	N	N	N	N	N	N	Y	N	N	Y	49	1.31	1.04	27.13	151	47	136	133	4.5	2.7	17.8/1.63	198	0.76
66	551484	HS	60/M	Y	N	N	Y	Y	N	N	N	N	N	3 years	ALD	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	Y	Y	28	1.24	1.41	10.3	141	27	129	139	4.3	3.45	17.4/1.59	77	0.1
67	987105	KD	55/F	Y	Y	Y	N	Y	N	N	N	N	N	RD	NASH	N	N	HTN, Hypothyroid	N	N	N	N	Y	N	N	N	N	N	Y	Y	Y	Y	55	1.6	1.46	29.08	135	66	429	121	4.2	2.45	17.4/1.59	154	0.3

		Investigations																																						
				Complete blood Count			Urine Routine Examination			Ultrasound										Other Investigations (positive)																				
S.No.	MRD No.	U.Spot Na	FENa	Haemoglobin	TLC	Platelets	Protein	RBC/HPF	Pus cells/HPF	Cirrhosis	CKD	VM	SBP	SAAG	Endoscopic Findings	Estimated Cr. Cl.	CTP (Score/ Class)	MELD	Urine C/S	Ascitic fluid C/S	Pleural fluid C/S	Blood C/S	ET Secretions C/S	Tropical fever	Amoebic Serology	PCT	Fungal Markers	Stool for C.diff	Recovery of AKI	Type of AKI	Mortality Outcome										
1	664602	15	0.2	7.6	4.7	96	Traces	N	N	Y	N	NR	N	1.82	Y	12	10/C	30	N	N	N	N	N	N	N	N	N	N	CR	HRS	Discharged										
2	702095	10	0.3	6.9	15	75	N	N	3 to 5	Y	N	NR	N	1.4	Y	59	14/C	30	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
3	635843	25	0.2	12.8	10	120	N	N	N	Y	N	HCV	N	1.42	N.D	40.72	12/C	39	N	N	N	N	N	N	N	N	N	N	PR	Pre	Expired										
4	724604	10	0.2	9.4	11	170	N	N	N	Y	N	NR	N	1.6	Y	23	12/C	39	Y	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
5	99602	20	0.1	11.9	8.9	130	N	60 to 65	N	Y	N	NR	N	N	Y	39	6/A	19	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
6	739039	18	0.4	11.2	8.4	150	N	35 to 50	5 to 6	Y	N	NR	Y	1.62	Y	44	8/B	24	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
7	749245	23	0.3	8.4	6.9	30	N	N	N	Y	N	HBV	Y	1.9	Y	56	11/C	34	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
8	759005	15	0	8.8	7.6	40	N	N	N	Y	N	HBV	N	N	N.D	36	11/C	40	Y	N	N	Y	N	N	N	N	N	N	CR	Pre	Discharged										
9	623666	22	0.9	7.8	8.1	162	N	N	10 to 12	Y	N	NR	N	2.06	Y	15	12/C	34	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
10	776699	17	0.2	12.3	30	278	N	N	N	Y	N	HCV	N	2.5	Y	70	10/C	30	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
11	236838	39	1.2	12.1	14	45	N	12 to 14	0 to 2	Y	N	NR	N	N	Y	23	8/B	34	Y	N	N	Y	N	N	N	N	N	N	CR	ATN	Discharged										
12	800391	12	0.2	3.8	16	246	N	5 to 8	N	Y	N	NR	N	N	Y	65	11/C	28	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
13	796914	66	1.4	10.7	12	70	N	4 to 5	N	Y	N	HBV	Y	2.05	Y	71	8/B	15	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
14	772784	12	0.4	12.8	7.1	110	N	N	N	Y	N	NR	N	2.29	Y	35	12/C	35	N	N	N	N	N	N	N	N	N	N	NR	Pre	Expired										
15	901546	21	1.5	10.2	14	110	N	30 to 35	N	Y	N	HBV	N	1.8	Y	10	10/C	30	N	N	N	N	N	N	N	N	N	N	PR	Int	Discharged										
16	444518	20	1.3	7.7	21	31	N	20 to 25	20 to 25	Y	N	NR	Y	2.04	Y	29	12/C	32	N	N	N	N	N	N	N	N	N	N	CR	Int	Discharged										
17	457248	15	0.4	10.4	11	84	N	N	N	Y	N	NR	N	2.31	Y	75	15/C	33	N	N	N	Y	N	N	N	N	N	N	CR	Pre	Discharged										
18	34255	36	1	7	8.1	22	N	40 to 45	N	Y	N	NR	N	1.6	Y	106	12/C	22	N	N	N	N	N	N	N	N	N	N	NR	Pre	Expired										
19	909397	35	1.2	13.6	35	208	N	N	N	Y	N	NR	N	1.4	Y	30	15/C	40	N	N	N	N	N	N	N	N	N	N	NR	ATN	Expired										
20	904288	85	17.4	9.6	18	162	N	5 to 8	N	Y	N	NR	N	1.23	Y	10	12/C	40	N	N	N	N	N	N	N	N	N	N	PR	Post	Expired										
21	761719	26	0.2	9.9	11	150	N	8 to 10	8 to 10	Y	N	NR	N	2.31	Y	79	12/C	19	Y	N	N	N	N	N	N	N	N	N	CR	HRS	Discharged										
22	885606	15	0.4	6.5	18	100	N	5 to 6	2 to 4	Y	N	NR	N	2.01	Y	34	13/C	34	N	N	N	N	N	N	N	N	N	N	NR	HRS	Expired										
23	910260	12	0.2	11.6	17	140	1+	35 to 40	45 to 50	Y	N	HCV	N	1.2	Y	42	7/B	22	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
24	903787	35	1.5	11.2	22	121	1+	30 to 35	N	Y	N	NR	N	1.29	Y	36	12/C	28	N	N	N	N	N	N	N	N	N	N	NR	ATN	Expired										
25	975399	34	0	9.6	8.4	80	N	N	N	Y	N	NR	N	1.56	Y	70	12/C	37	N	N	N	N	N	Y	N	N	N	N	PR	Pre	Discharged										
26	976336	63	1.1	8.9	13	59	N	4 to 5	8 to 10	Y	N	NR	N	N	Y	33	11/C	39	N	N	N	N	N	N	N	N	N	N	PR	Int	Expired										
27	971562	29	1.1	9.7	22	150	N	N	3 to 5	Y	N	NR	N	2.9	Y	48	11/C	33	N	N	N	N	N	N	N	N	N	N	NR	ATN	Expired										
28	963735	14	0.5	8.3	13	150	N	N	N	Y	N	NR	N	N	Y	36	7/B	18	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
29	979729	10	0.2	8.1	20	67	N	N	N	Y	N	HCV	N	1.8	Y	26	14/C	40	N	N	N	N	N	N	N	N	N	N	NR	HRS	Expired										
30	640959	47	1.6	10.5	9.7	123	1 +	70 to 80	6 to 8	Y	N	NR	N	1.2	Y	28	10/C	24	N	N	N	N	N	N	N	N	N	N	CR	ATN	Discharged										
31	976443	31	1.7	12.8	17	265	2 +	10 to 12	15 to 20	Y	N	NR	N	N	N.D	39	11/C	32	N	N	N	N	N	N	N	N	N	N	NR	ATN	Expired										
32	979671	20	0.7	8	7.4	164	N	2 to 3	N	Y	N	HBV	N	1.4	Y	29	11/C	30	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
33	972222	17	0.4	11.1	24	234	Traces	20 to 25	N	Y	N	NR	N	2.05	Y	33	13/C	40	N	N	N	N	N	N	N	N	N	N	CR	HRS	Discharged										
34	923948	7	0.1	12.8	9.1	41	N	N	N	Y	N	NR	N.D	N.D	Y	46	11/C	31	N	N	N	N	N	Y	N	N	N	N	CR	Pre	Discharged										
35	965402	42	1.4	10.1	25	98	N	N	N	Y	N	HCV	Y	1.9	Y	28	12/C	36	N	N	N	N	N	N	N	N	N	N	NR	ATN	Expired										
36	980716	12	0.1	5.3	20	171	Traces	8 to 10	N	Y	N	NR	N	2.3	Y	104	11/C	23	N	N	N	N	N	N	N	N	N	N	NR	Pre	Expired										
37	980418	37	0.3	6.1	13	70	N	N	N	Y	N	NR	N	N	N	54	7/B	21	N	N	N	N	N	Y	N	N	N	N	CR	Pre	Discharged										
38	982231	55	3	7.8	26	90	1+	2 to 4	N	Y	N	NR	Y	1.2	N.D	33	11/C	29	N	N	N	N	N	N	N	N	Y	N	NR	ATN	Expired										
39	980523	36	0.7	12.1	24	153	N	N	N	Y	N	NR	Y	2.39	Y	54	13/C	31	N	N	N	N	N	N	N	Y	Y	N	CR	Pre	Discharged										
40	84322	19	0.2	12.4	6.9	113	N	N	N	Y	N	NR	N	N	Y	49	9/B	22	Y	N	Y	N	N	N	N	N	N	N	CR	Pre	Discharged										
41	980279	12	0.3	8.1	6.2	96	N	N	N	Y	N	HCV	N	2.56	Y	45	8/B	19	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
42	981092	35	0.4	10.5	23	150	1+	8 to 10	4 to 6	Y	N	NR	N	2.21	Y	91	13/C	33	N	N	N	N	N	Y	N	N	N	N	NR	HRS	Expired										
43	31095	31	0.6	7.9	2.2	38	N	N	N	Y	N	NR	N	N	Y	30	14/C	35	N	N	N	N	N	N	N	Y	N	N	CR	Pre	Discharged										
44	979674	19	0.9	9.6	21	160	Traces	10 to 12	N	Y	N	NR	N	N	N	87	9/B	24	N	N	N	Y	N	N	N	N	N	N	CR	Pre	Discharged										
45	977726	17	0.2	8.6	40	137	1+	N	4 to 6	Y	N	NR	Y	1.74	Y	30	11/C	30	N	N	N	N	N	N	N	N	N	Y	CR	Pre	Discharged										
46	981651	12	0.4	5.6	32	51	N	30 to 40	2 to 4	Y	N	NR	Y	1.44	N	20	13/C	36	N	N	N	N	N	N	N	Y	N	N	CR	Pre	Discharged										
47	531835	63	3.5	3.8	5.8	50	Traces	N	N	Y	N	NR	N	N	Y	32	8/B	13	N	N	N	N	N	N	N	Y	N	N	CR	ATN	Discharged										
48	983526	127	7	6.7	11	70	N	10 to 12	N	Y	N	HCV	N	N	N.D	53	7/B	19	N	N	N	N	N	Y	N	N	N	N	CR	Post	Discharged										
49	983511	27	0.6	8.7	7	139	N	N	N	Y	N	NR	Y	2.06	Y	65	9/B	14	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
50	981142	9	0.2	6.1	4.3	60	N	N	N	Y	N	NR	Y	1.03	Y	58	11/C	21	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
51	934040	16	0.1	10.9	17	126	N	N	N	Y	N	HBV	N	1.5	N.D	45	9/B	25	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
52	984336	20	0.8	8.2	19	150	Traces	N	N	Y	N	HCV	N	2.1	Y	51	10/C	20	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
53	984199	11	0.1	10.7	7.5	50	N	N	N	Y	N	NR	N	2.76	Y	79	8/B	16	N	N	N	N	N	N	N	N	N	N	CR	HRS	Discharged										
54	648172	109	3.3	9.2	6.6	196	3+	10 to 12	60 to 70	Y	N	NR	N	1.24	Y	31	9/B	19	Y	N	N	N	N	N	N	N	N	N	PR	ATN	Discharged										
55	984060	41	0.6	6	5.9	50	N	N	N	Y	N	NR	N	1.66	Y	39	13/C	33	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
56	861457	23	0.2	5.8	5.7	72	N	N	N	Y	N	NR	N	1.5	Y	24	9/B	32	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
57	757398	36	1.2	4.3	25	379	2+	5 to 8	4 to 6	Y	N	NR	N	2.27	Y	22	13/C	36	N	N	N	N	N	N	N	N	N	N	NR	ATN	Expired										
58	873542	13	0.3	10.9	20	157	N	N	5 to 6	Y	N	NR	N	1.92	N.D	22	14/C	34	N	N	N	N	N	N	N	N	N	N	NR	Pre	Expired										
59	68025	26	0.1	10.3	6.1	24	2+	15 to 18	30 to 35	Y	N	NR	N	2.26	N.D	62	10/C	20	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
60	873667	16	0.2	11.8	16	170	N	N	N	Y	N	NR	N	2.05	N.D	75	9/B	16	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
61	509550	9	0.1	9.2	3.2	83	Traces	N	6 to 8	Y	N	NR	N	1.9	Y	62	6/A	20	N	N	N	N	N	N	N	N	N	N	PR	HRS	Discharged										
62	875369	13	0.2	10.2	11	57	N	N	8 to 10	Y	N	NR	N	2	Y	51	11/C	31	N	N	N	Y	N	N	N	N	N	N	CR	Pre	Discharged										
63	913187	31	0.1	9.3	10	211	N	N	N	Y	N	NR	N	1.5	N	104	9/B	17	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										
64	978943	27	0.4	3.3	14	94	N	N	N	Y	N	NR	Y	2.17	Y	75	13/C	26	N	N	N	Y	N	N	N	Y	N	N	CR	Pre	Discharged										
65	988775	70	0.8	9.4	16	234	1+	N	N	Y	N	NR	N	1.78	N.D	86	11/C	29	N	N	N	N	N	N	N	N	N	N	NR	Pre	Expired										
66	551484	74	0.6	10.7	8.9	60	Traces	N	N	Y	N	NR	N	3.21	Y	79	12/C	22	N	N	N	N	N	Y	N	N	N	N	CR	Pre	Discharged										
67	987105	10	0.1	13.1	14	134	Traces	N	N	Y	N	NR	N	2.28	N.D	50	10/C	33	N	N	N	N	N	N	N	N	N	N	CR	Pre	Discharged										

				Presenting Complaints											Past History					Drug History									GPE			Systemic Examination																	
															Cirrhosis																																		
S.No.	MRD No.	Name	Age/Sex	Jaundice	Edema	AD	H/M	AS	Fever	PA	Vomiting	ABH	DUO	Duration	Etiology	J	VB	CoNmorbidities	Diuretics	Laxatives	NSAIDs	Comp & Alt Med	Nephrotoxic Antibiotics	Beta Blockers	Antiplatelet + Statin	Contrast	OHA	Shock	J	E	Flaps	P/A (FF)	Urea	S.Cr (Day 1)	S.Cr. (Day 3)	Total Bilirubin	SGOT	SGPT	ALP	Na	K	S.Alb	PTI/INR	Ammonia	UPCR
68	948996	GS	62/M	N	Y	Y	N	N	N	N	N	Y	Y	7 months	NASH	N	Y	DM II, HTN	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	81	1.96	1.66	2.49	207	62	310	132	4.8	2.62	14.4/1.32	137	0.19
69	473700	PKB	69/M	N	N	N	N	N	Y	Y	N	N	N	10 years	NASH	Y	Y	DM II	N	N	N	N	N	Y	N	N	Y	Y	N	N	N	N	89	1.61	1.48	1.45	50	48	110	135	4.1	2.55	15.4/1.41	N.D	0.12
70	64479	BS	65/M	N	N	Y	N	Y	N	N	N	N	N	6 months	HCV	N	N	N	Y	N	N	N	N	Y	N	N	N	N	N	N	Y	Y	96	3.13	2.82	2.01	38	14	128	140	3.8	2.91	15.0/1.38	156	0.077
71	901585	KS	68/M	N	Y	N	Y	N	N	N	N	N	N	2 years	NASH	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	34	1.28	1.16	1.89	43	26	190	144	4.3	3.1	17.3/1.59	N.D	0.1
72	988101	Y	62/M	N	N	Y	N	N	Y	N	N	N	N	15 years	ALD	Y	Y	DM II	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	65	1.31	1.27	2.83	41	22	114	127	4.5	2.43	15.8/1.44	84	0.28
73	989652	RK	48/M	Y	N	Y	N	Y	N	N	N	Y	Y	6 years	NASH +ALD	N	Y	Obesity	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	83	1.98	1.57	0.67	21	7	84	140	4.4	2.53	13.8/1.26	207	0.97
74	543386	NS	65/M	N	N	Y	Y	N	N	N	Y	N	N	2 years	HBV+ALD	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	174	2.52	1.25	0.74	62	21	96	129	6	2.92	15.1/1.38	N.D	0.147
75	873477	AS	56/M	Y	N	N	N	N	N	N	N	Y	N	12 years	HCV	Y	N	DM II	Y	N	N	N	N	N	N	N	N	N	Y	N	Y	N	145	2.09	2.05	42.77	113	39	185	133	3.5	2.84	17.1/1.56	334	0.6
76	894166	BK	75/M	N	N	Y	N	N	N	N	N	Y	N	10 years	Autoimmune	Y	Y	CAD	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	26	1.3	1.4	0.9	50	22	81	136	3.9	2.89	13.1/1.20	N.D	0.2
77	945825	MS	51/M	Y	Y	Y	N	N	Y	Y	N	N	N	6 months	ALD	Y	N	Old SAH	Y	N	N	N	N	N	N	N	N	N	Y	Y	N	Y	60	1.33	0.89	15.77	155	85	128	125	4.9	3.58	21.5/1.96	52	0.15
78	981842	IS	56/M	Y	Y	Y	N	Y	N	N	N	N	Y	RD	ALD	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	83	2.54	1.4	6.7	384	172	234	135	4.6	2.34	13.7/1.25	61	0.3
79	187319	GS	58/M	Y	N	Y	Y	N	Y	Y	N	N	Y	8 years	ALD	N	Y	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	Y	146	2.8	3.12	8.29	59	19	218	136	4.8	2.51	15.3/1.40	65	0.4
80	986538	RC	68/M	Y	Y	Y	N	N	N	N	N	N	N	RD	ALD + NASH	N	N	HTN, Obesity	N	N	N	N	N	N	N	N	N	Y	Y	Y	N	Y	37	1.41	2.04	29.25	259	95	215	121	4.9	2.45	16.4/1.50	103	0.52
81	456804	KKG	72/M	Y	Y	Y	N	Y	N	Y	Y	Y	Y	32 years	HCV	Y	Y	_	N	N	N	N	N	N	N	N	N	N	Y	Y	N	Y	206	3.14	2.99	11.52	302	189	520	129	4.4	3.16	19.6/1.79	140	0.3
82	990350	AK	34/M	Y	N	Y	N	N	N	Y	Y	N	Y	1 month	NASH	N	N	N	Y	N	Y	Y	N	N	N	N	N	N	Y	N	N	Y	113	5.92	6.3	11.36	87	31	122	126	4.2	2.5	19.8/1.81	197	0.73
83	898668	JS	35/M	N	N	Y	N	N	N	Y	N	N	Y	3 years	ALD	Y	N	N	Y	N	N	Y	N	N	N	N	N	N	N	Y	Y	Y	50	1.49	1.1	0.81	82	12	335	138	4.2	1.69	11.8/1.08	124	0.5
84	938046	MP	62/M	Y	Y	Y	Y	N	Y	N	N	Y	Y	7 months	ALD	Y	N	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	41	1.33	1.04	4.66	87	35	116	139	4.7	2.86	18.3/1.67	N.D	0.07
85	926358	BS	37/M	Y	N	Y	N	N	Y	N	N	N	Y	4 years	ALD	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	Y	59	2.5	6.3	17.7	279	1058	217	147	5.6	2.4	54/6.0	N.D	0.7
86	6789	MS	35/M	N	N	N	Y	Y	N	N	Y	N	Y	1 year	ALD	N	Y	N	N	N	N	N	N	N	N	N	N	Y	N	N	Y	N	76	3.2	4.6	2.4	800	948	140	150	5.5	2.2	36.2/2.9	90	0.3
87	896664	RK	46/M	N	N	N	N	Y	Y	Y	Y	Y	Y	6 months	ALD	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	Y	N	97	2.8	3.2	1.7	560	258	500	142	3.6	3.4	20.1/1.9	120	0.6
88	567359	KA	35/F	N	N	N	N	Y	Y	N	Y	Y	Y	RD	Autoimmune	N	N	Hypothyroid	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	56	1.8	0.78	1.2	86	94	124	129	3.3	3.2	19.6/1.78	90	0.2
89	46857	PS	48/M	Y	Y	Y	N	Y	Y	N	N	N	Y	4 years	ALD	Y	N	HTN	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	67	3.3	1.6	21.6	104	95	193	116	4.6	2.4	20.1/2.6	180	0.3
90	874569	GS	55/M	N	N	Y	Y	N	N	N	Y	N	Y	RD	ALD + HCV	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	246	2.5	1.9	1.8	53	36	122	137	6.2	2.2	21.3/1.9	N.D	0.5
91	64521	AK	60/F	Y	Y	Y	N	Y	Y	Y	Y	N	Y	10 years	HBV	Y	N	HTN	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	165	3.6	5.2	10.5	265	458	780	125	5.5	1.9	38.9/3.2	360	1.2
92	795486	JS	31/M	Y	N	N	N	Y	Y	Y	N	N	Y	6 months	HBV	Y	N	N	N	N	N	Y	N	N	N	N	N	N	Y	N	Y	N	142	2.54	5.6	22.1	94	105	152	127	3.8	3.2	18.4/1.52	245	0.8
93	5687	PS	36/M	N	N	N	N	N	Y	Y	Y	Y	Y	2 years	ALD	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	120	1.8	1.18	2.4	231	157	89	141	2.9	3.8	16.5/1.2	N.D	0.1
94	984532	JK	62/F	N	N	Y	Y	Y	N	N	Y	Y	N	15 years	HCV	Y	Y	DM II	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	123	5.9	7.3	4.6	216	223	64	129	4.4	2.6	21/1.8	230	0.4
95	887769	HK	29/F	Y	Y	N	N	N	Y	Y	Y	Y	Y	RD	Autoimmune	N	N	Celiac disease	N	N	N	Y	N	N	N	N	N	N	Y	Y	N	N	256	2.9	2.4	18.4	46	58	187	138	5.9	2.3	23.6/2.2	N.D	0.1
96	956472	RL	72/M	N	Y	Y	N	N	Y	N	Y	Y	Y	20 years	NASH	Y	Y	N	N	N	N	N	N	N	Y	N	N	N	Y	Y	Y	Y	78	2.1	1.8	2.2	75	58	140	141	3.8	2.1	18.6/1.7	N.D	0.5
97	7564	AJ	57/M	Y	Y	Y	N	N	Y	Y	Y	N	Y	5 years	ALD	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	N	Y	152	4.8	6.4	15.3	450	586	972	150	5.6	1.9	21.4/2.01	N.D	1.6
98	897216	FP	62/M	N	Y	Y	N	N	Y	Y	Y	N	N	10 years	ALD	Y	Y	DM II	N	N	N	N	N	N	N	N	N	N	N	Y	N	Y	67	1.8	1.3	1.7	45	67	153	138	4.1	2.1	19.3/2.1	N.D	0.6
99	5648	NS	54/M	Y	Y	Y	N	Y	Y	N	N	N	Y	5 years	NASH	N	N	DM II, Obesity	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	16	2.7	3.2	7.4	598	192	87	137	5.2	1.9	33.1/3.3	82	0.7
100	978246	BS	37/M	N	N	N	N	N	Y	Y	Y	Y	N	4 months	ALD	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	53	1.8	1.02	1.2	49	46	76	131	3.1	3.2	18.2/1.6	N.D	0.3

| S.No. | MRD No. | Investigations | | | | | | | | | | | | | | | | | | Other Investigations (positive) | | | | | | | | | | | | | | | | | |

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The Principal,
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Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.05.2019 has approved the plan of thesis of **Anureet**, a student of your college for **MD General Medicine** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis

To study the spectrum of renal dysfunction in admitted patients with liver cirrhosis

Supervisor
Dr. Vikas Garg
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Co-Supervisor
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The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

SP Singh

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

TO STUDY THE SPECTRUM OF RENAL DYSFUNCTION IN ADMITTED PATIENTS WITH LIVER CIRRHOSIS

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DOCTOR OF MEDICINE

In

MEDICINE

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

SEPTEMBER, 2018 DR. ANUREET

DEPARTMENT OF MEDICINE

DAYANAND MEDICAL COLLEGE AND HOSPITAL

LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	TO STUDY THE SPECTRUM OF RENAL DYSFUNCTION IN ADMITTED PATIENTS WITH LIVER CIRRHOSIS
For the degree of	M.D MEDICINE
Name of the candidate	Dr. Anureet
Supervisor	Dr. Vikas Garg, Professor Department of Medicine, Dayanand Medical College and Hospital, Ludhiana
Co-supervisor	Dr. Omesh Goyal, Associate Professor, Department of Gastroenterology, DMCH, Ludhiana Dr. Preet Mohinder Singh, Assistant Professor, Department of Nephrology, DMCH, Ludhiana
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Renal dysfunction is a common complication in patients of liver cirrhosis and of utmost clinical and prognostic relevance. Chances of development of acute kidney injury (AKI) are more in patients with cirrhosis than the non-cirrhotic population. Most common causes of AKI in cirrhosis include pre-renal AKI, the hepatorenal syndrome type of AKI (HRS-AKI, formerly known as 'type 1') and acute tubular necrosis. Differentiation is important as treatment differs substantially. While pre-renal AKI usually responds well to plasma expansion, HRS-AKI and ATN require different specific approaches and are associated with substantial mortality.

Aim of Study: To study the clinical profile of renal dysfunction in admitted patients with liver cirrhosis.

Materials & methods: This study will include 100 consecutive patients of age ≥ 18 years admitted in Dayanand Medical College and Hospital, Ludhiana with liver cirrhosis & are found to have renal dysfunction.

Clinical Significance: This study will help us in documenting the common causes of renal involvement in liver cirrhosis and in planning further investigation and management of these patients.

Keywords: liver cirrhosis, acute kidney injury, acute tublar necrosis, hepatorenal syndrome.

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled "**TO STUDY THE SPECTRUM OF RENAL DYSFUNCTION IN ADMITTED PATIENTS WITH LIVER CIRRHOSIS**" exist in the Department of Medicine, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

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Place: LUDHIANA

Date: 29/12/2018

APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
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Name of candidate	Dr. Anureet
Department	Medicine
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Likely date of appearing in PG examination	May 2021
Date of enrollment	10 May, 2018
Name of Head of Department	Dr. Dinesh Gupta
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1. HOD Pharmacology	1. HOD Physiology
2. HOD Surgery	2. HOD Pathology
3. HOD Pathology	3. HOD Pharmacology
4. HOD Medicine	4. HOD SPM
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6. Vice Principal	6. HOD Surgery
	7. HOD Obst. & Gynae
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	9. Secretary, IEC
	10. Dean Academics
	11. Vice Principal
	12. Principal

Approved: Yes / No

Chairperson
Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

Chairperson
Ethics Committee

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PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. Anureet H. No. 828, Ekta Nagar Phase -1, Rama Mandi, Jalandhar Cantt., Jalandhar, Punjab
2	NAME OF THE INSTITUTE	Dayanand Medical College and Hospital, Ludhiana
3	COURSE OF STUDY AND SUBJECT	MD Medicine
4	DATE OF ADMISSION OF COURSE	10th May 2018
5	TITLE OF THE TOPIC	"TO STUDY THE SPECTRUM OF RENAL DYSFUNCTION IN ADMITTED PATIENTS WITH LIVER CIRRHOSIS"

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Acute kidney injury (AKI) is frequently observed in hospitalized patients with cirrhosis and is associated with increased mortality. AKI has an estimated prevalence of approximately 20-50% among hospitalized patients with cirrhosis [1] and patients with cirrhosis are more likely to develop renal failure compared to individuals without liver disease.[2] AKI is associated with poor prognosis and represents an important predictor for short-term mortality in patients with cirrhosis.[3] The occurrence of AKI, irrespective of the underlying cause, is associated with reduced in-hospital, 3-month and 1-year survival. Hepatorenal syndrome is associated with the worst outcome among AKI patients with cirrhosis.[4]

Renal failure is a common complication of decompensated cirrhosis. AKI occurs in 11% of patients with upper gastrointestinal bleeding, in 34% of patients with spontaneous bacterial peritonitis (SBP), in 27% with bacterial infections other than SBP and in 40% to 49% of critically-ill patients with cirrhosis requiring intensive care support.[5,6] Furthermore, 24% of outpatients with cirrhosis develop some type of renal failure within one year of the first episode of ascites.[7] In most reports, renal failure significantly reduces survival rates.[6,7]

With an yearly incidence of 8-12%, HRS-AKI is quite common in decompensated cirrhosis with ascites.[8] The correct classification of AKI is essential since HRS-AKI, representing one of the most lethal complications of portal hypertension, requires a specific treatment approach. However, despite

adequate treatment, mortality is still about 60% and higher.[9] HRS-AKI is a diagnosis by exclusion and thus, often difficult to establish.

Approximately 40% of patients experience AKI during their hospitalization with the majority of cases having been diagnosed at stage 1. Also, in patients with AKI stage 1 and a sCr of < 1.5 mg/dl already a 3.5-fold increase in 30-day mortality as compared to patients without AKI was reported [10], again underlining the prognostic importance of even small increases in sCr levels.

Majority of clinical studies focused their attention on HRS, which is mostly present in advanced stages of cirrhosis. However, other forms of renal disorders in cirrhotic patients have equal importance in view of their incidence and prognostic impact in such patients.

There are limited studies describing various renal disorders & their prognostic impact in patients with cirrhosis of liver. The aim of this work is to study the clinical spectrum of renal disorders in patients with cirrhosis of liver and their prognostic impact.

The exact incidence of renal disorders in patients with cirrhosis is largely unknown and probably underestimated. Most of these studies are retrospective and/or they address only a particular subset of renal disorders [e.g., acute kidney injury and/ or hepatorenal syndrome (HRS)] rather than the whole spectrum of renal diseases that occurs in cirrhotic patients.

This hospital based study will look into the incidence, etiology, and spectrum of renal disorders in patients with cirrhosis of liver and their impact on prognosis.

6.2 REVIEW OF LITERATURE

The first reports of renal failure in the setting of cirrhosis of liver were from Europe and the United States in the late nineteenth century.[11] Hecker and Sherlock in 1956 gave the first detailed description of HRS.[12] Vesin [13] and Koppel et al [14] later established the functional nature of this renal disease. Since then, the relationship between the liver and kidney functions has been an object of great research efforts. Garcia-Tsao et al [15], in a recent meta-analysis, reported that the incidence of renal disease was 27% in their cirrhotic patients.

The spectrum of causes for AKI in cirrhosis includes:

i. Prerenal AKI (i.e. hypovolemia due to gastrointestinal bleeding, aggressive diuretic treatment, lactulose-induced diarrhea or infections).

ii. The hepatorenal syndrome-type AKI (HRS-AKI), which is defined as a potentially reversible deterioration of renal function unresponsive to volume resuscitation, caused by renal vasoconstriction in the absence of alternative identifiable causes.[16,17]

iii. Intrinsic causes such as acute tubular necrosis and, although very rare,

iv. Postrenal causes.

CURRENT DIAGNOSTIC CRITERIA FOR AKI:

KDIGO CRITERIA FOR AKI (2012):[15]

AKI is defined as any of the following (not graded):

- Increase in SCr by $\geq$ 0.3 mg/dl ($\geq$ 26.5 µmol/l) within 48 hours; or
- Increase in SCr to $\geq$ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume < 0.5 ml/kg/h for 6 hours.

- **STAGING OF AKI**

Stage	Serum Creatinine	Urine Output
1	1.5 – 1.9 times baseline OR ≥ 0.3 mg/dl (≥ 26.5 µmol/l) increase	<0.5 ml/kg/h for 6-12 hours
2	2.0 – 2.9 times baseline	<0.5 ml/kg/h for ≥ 12 hours
3	3.0 times baseline OR Increase in serum creatinine to ≥ 4.0 mg/dl (≥ 353.6 µmol/l) OR Initiation of renal replacement therapy OR, In patients < 18 years, decrease in eGFR to <35 ml/min per 1.73 m^2	<0.3 ml/kg/h for ≥ 24 hours OR Anuria for ≥ 12 hours

The main modifications over the former, rather stringent criteria that were based on absolute serum creatinine level, was abandoning the arbitrary threshold of sCr > 1.5 mg/dl to diagnose AKI, since milder degrees of renal failure in patients with cirrhosis had often remained underdiagnosed.[19] In addition, the use of urine output as part of the diagnostic criteria was eliminated, since many patients with cirrhosis and ascites maintain a preserved renal function despite being oliguric due to sodium and water retention.[20]

HRS type of AKI (HRS-AKI, formerly known as type 1 HRS)

The first consensus conference on a uniform definition for hepatorenal syndrome (HRS) took place in 1978 in Sassary, Italy.[21] HRS was then considered an acute renal dysfunction associated with extensive renal sodium water retention associated with acute or chronic liver disease. However, the evolving understanding of the pathophysiology of HRS has led to several reclassification and redefinitions.[16,21]

The hepatorenal syndrome type of AKI (HRS-AKI) is defined as ≥ stage 2 AKI that is diagnosed after other causes of renal failure have been ruled out.[20]

DIAGNOSTIC CRITERIA OF HEPATORENAL SYNDROME [20]

- Presence of cirrhosis and ascites
- No improvement in serum creatinine after 2 consecutive days of withdrawal of diuretics and plasma expansion with albumin (1g per kg of body weight, maximum 100 g/day)
- Absence of shock
- Exclusion of recurrent or recent use of nephrotoxic drugs (e.g. NSAIDs, aminoglycosides, contrast media)
- Exclusion of parenchymal kidney disease:
  - Absence of proteinuria (>500 mg/day)
  - Absence of microhematuria (>50 RBCs per high-power field)
  - Normal renal ultrasonography

Hepatorenal syndrome type 2 (hepatorenal syndrome type of chronic kidney disease)

Type 2 HRS is characterized by a stable or slowly progressive impairment in renal function in patients with decompensated liver disease who suffer from refractory ascites.[16] Apart from the time of development, the same specific diagnostic criteria for HRS-AKI also apply for HRS type 2.[22] In general, prognosis in HRS type 2 is poor, but more favourable when compared to AKI-HRS.[23]

A systemic review of studies which evaluated the predictors of survival in cirrhosis have reported that parameters of renal dysfunction (creatinine and blood urea nitrogen/ azotemia) together with parameters of liver dysfunction

(Child – Pugh score and its components) were important predictors of death in decompensated cirrhosis.[24]

6.3 AIMS AND OBJECTIVES OF THE STUDY

1. To study the clinical profile of renal dysfunction in admitted patients with liver cirrhosis.

7. MATERIALS AND METHODS

This study will include 100 consecutive patients of age ≥ 18 years admitted in Dayanand Medical College and Hospital, Ludhiana with liver cirrhosis and are found to have renal dysfunction.

7.1 SOURCE OF DATA:

This study will include 100 consecutive patients of liver cirrhosis admitted in the Department of Medicine and Allied Super specialities of Dayanand Medical College and Hospital, Ludhiana who will be having renal dysfunction.

7.2 METHOD OF COLLECTION OF DATA

All the patients included in this study will be assessed as follows-

1-Clinical assessment

Detailed history of presenting complaints will be taken.

Relevant past, personal, drug history and family history will also be taken

Findings of general and systemic findings will be recorded.

2- Laboratory investigations

The results of routine investigations like CBC, RFT, LFT, RBS, Urine routine, CXR, ECG will be recorded in all cases.

The results of PTI/INR, ESR, Arterial Ammonia, USG Abdomen, Ascitic fluid analysis, relevant C/S, viral markers will also be recorded. The results of urinary protein to creatinine ratio, spot urinary sodium, and other investigations for renal dysfunction will be recorded.

Investigations like ABG, Upper GI Endosopy, Fibroscan will be optional and done wherever indicated.

INCLUSION CRITERIA – Presence of all of the following –

- Age ≥ 18 years
- Those willing to give consent
- Diagnosed cases of cirrhosis based on history, examination, LFTs, USG Abdomen & Fibroscan (wherever indicated).
- Renal dysfunction suggestive of AKI as per KDIGO criteria (2012).

EXCLUSION CRITERIA –

- Pregnant females
- Patients of chronic renal failure will be excluded based on history, examination and USG showing small kidneys.
- Patients of liver cirrhosis having renal involvement previously enrolled in this study and are readmitted will be excluded.

OUTCOME: The outcome will be recorded as under-

a) Outcome of the patient at the end of hospital stay – Discharged/ Death

b) Recovery of renal dysfunction at the end of hospital stay – Not recovered/ partially recovered/ completely recovered.

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

NO

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith

8. REFERENCES

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PROFORMA

Serial no. **Name** **Age/Sex**

MRD No. **Admission no.** **DOA**

Contact Info.-

History of present illness: **Duration**

- Jaundice yes/no
- Edema yes/no
- Abdominal distension yes/no
- Haemetemesis/ Malaena yes/no
- Altered sensorium yes/no
- Fever yes/no
- Pain abdomen yes/no
- Vomiting yes/no
- Altered bowel habits yes/no
- Decreased urine output yes/no

Past History

- Chronic Liver disease Duration- Etiology (if known)-
- Jaundice (yes/no) Episodes Duration
- Variceal bleed (yes/no) Episodes Endoscopy
- Co-morbidities
- Any other relevant history

Personal History

- Alcoholic (yes/no) Type Amount Duration
- Smoker (yes/no) Type Amount Duration
- Substance abuse (yes/no) Type Amount Duration

Signature of Candidate **Signature of Supervisor**

Drug history / Nephrotoxic drugs

- Name Dose Frequency Duration

Family History:

General Physical Examination:

Sensorium-

P I CY CL JVP LAN E Skin Changes

Others

- **Vitals:**

  PR BP RR O_2 Sat Temperature

- **Systemic Examination**
  - Per abdomen examination:
    - Shape
    - Caput medusae
    - Visible veins
    - Tenderness
    - Organomegaly
    - Bowel sounds
  - Chest examination:
  - CVS examination:
  - CNS examination:
    - Sensorium
      - Grade of encephalopathy
    - Flaps
    - Apraxia charting

Signature of Candidate **Signature of Supervisor**

Investigations:

INVESTIGATION/ DAY				
Haemoglobin	(gm/ dL)			
TLC	(10^3/ µL)			
DLC (P/L/M/E)	(%)			
Platelets	(10^3/ µL)			
RBS	(mg/ dL)			
ESR				
S. Urea	(mg/ dL)			
S. Creatinine	(mg/ dL)			
S. $Na^+/K^+/Cl^-$	(mmol/ L)			
T. Bilirubin	(mg/ dL)			
D. Bilirubin	(mg/ dL)			
SGOT	(U/L)			
SGPT	(U/L)			
ALP	(U/L)			
S. Proteins	(g/ dL)			
S. Albumin	(g/ dL)			
PTI/INR	(sec)			
Urine Routine				
Ammonia Estimation	(µmol/L)			
Urinary Protein to Creatinine Ratio				
Estimated Creatinine Clearance	(m L/ min)			
Spot Urinary Sodium	(mmol/L)			

Signature of Candidate **Signature of Supervisor**

FE_{Na}	(%)			
Relevant Culture/ Sensitivity				
Ascitic Fluid Analysis • Biochemistry • Cytology • Gram Stain • Culture/ Sensitivity • Others				
SAAG	(g/ dL)			
Viral Markers Hepatitis B Hepatitis C				
USG Abdomen				
ECG				
Chest X Ray				
ABG (optional)				
Upper G.I. endoscopy (optional)				
Fibroscan (wherever indicated)				
CTP Score/ Class				
Special investigations for etiology of cirrhosis (wherever indicated)				

URINE OUTPUT			

Signature of Candidate

Signature of Supervisor

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....

.....am willing to participate in the study **"TO STUDY THE SPECTRUM OF RENAL INVOLVEMENT IN ADMITTED PATIENTS WITH LIVER CIRRHOSIS"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

.....
Signature of the Witness

Name:

.....
Signature of the patient

Signature of Candidate

Signature of Supervisor

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य "**TO STUDY THE SPECTRUM OF RENAL INVOLVEMENT IN ADMITTED PATIENTS WITH LIVER CIRRHOSIS**" में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"TO STUDY THE SPECTRUM OF RENAL INVOLVEMENT IN ADMITTED PATIENTS WITH LIVER CIRRHOSIS" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ